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Inventors (please provide full names): _____

Earliest Priority Date: 10/28/98

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L1 593 S E3,E19
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L2 29 S E4,E5
E KLEKOTA B/AU
L3 5 S E4
L4 5 S L1,L2 AND L3
L5 622 S L1-L3
L6 39 S L5 AND 10506/CC
E CHEM/IT
E CHEM/CC
E CHEM/CT
L7 7 S L5 AND LIGAND
L8 4 S L6 AND L7
L9 6 S L4,L8
L10 2 S L7 NOT L9
L11 1 S L9 NOT L4
L12 1 S L10 NOT AB/FA
L13 6 S L4,L12
L14 2 S L7,L9 NOT L13
L15 34 S L6 NOT L7-L14
L16 6 S L5 AND LIBRARY
L17 6 S L16 AND L13
L18 5 S L16 AND L9
L19 6 S L17,L18

FILE 'BIOSIS' ENTERED AT 09:38:37 ON 27 MAR 2000

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L19 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:476363 BIOSIS
DN PREV199900476363
TI Selection of DNA-binding compounds via multistage molecular evolution.
AU **Klekota, Bryan; Miller, Benjamin L. (1)**
CS (1) Department of Chemistry, University of Rochester, Rochester, NY, 14627 USA
SO Tetrahedron, (Sept. 24, 1999) Vol. 55, No. 39, pp. 11687-11697.
ISSN: 0040-4020.
DT Article
LA English
SL English
AB Combinatorial **libraries** incorporating multiple equilibria offer opportunities to study molecular evolution, and are a novel method of identifying ligands for biological receptors. We describe the construction and evaluation of a multi-equilibrium combinatorial **library**, in

which structural diversity and structural mutation are accomplished via reversible imine formation and transition-metal complexation. We demonstrate that oligo d(AcntdotT)-cellulose resin can select subsets of this libray, in accord with measured solution-phase affinities.
CC Biochemical Methods - General *10050
Evolution *01500
Biophysics - General Biophysical Studies *10502
IT Major Concepts
Biochemistry and Molecular Biophysics; Evolution and Adaptation; Methods and Techniques
IT Chemicals & Biochemicals
DNA-binding compound: selection, synthesis
IT Methods & Equipment
multi-equilibrium combinatorial **library** technique: synthesis/modification techniques, synthetic method; multistage molecular evolution techniques: analytical method, receptor ligand identification
IT Miscellaneous Descriptors
molecular diversity generation; molecular evolution

L19 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:351293 BIOSIS
DN PREV199900351293
TI Dynamic diversity and small-molecule evolution: A new paradigm for **ligand** identification.
AU **Klekota, Bryan (1); Miller, Benjamin L. (1)**
CS (1) Department of Chemistry, University of Rochester, Rochester, NY, 14627 USA
SO Trends in Biotechnology, (May, 1999) Vol. 17, No. 5, pp. 205-209. ISSN: 0167-7799.
DT Article
LA English
SL English
AB A longstanding goal of organic, medicinal and bioorganic chemists has been the discovery of efficient methods for designing or identifying biologically active compounds. Recently, several groups have reported using the directed evolution of combinatorial **libraries** as a new method of identifying compounds capable of binding tightly to a target molecule. Although significant development remains to be done, the initial results suggest that dynamic diversity and associated selection methods will prove to be valuable additions to the drug-discovery process.
CC Pharmacology - General *22002
Evolution *01500
Comparative Biochemistry, General *10010
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology
IT Chemicals & Biochemicals
ligands: identification; small molecules
IT Miscellaneous Descriptors
drug discovery; dynamic diversity; evolutionary systems; photochemistry; small molecule evolution

L19 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:166007 BIOSIS
DN PREV199900166007
TI Evolving combinatorial **libraries** as a novel method for **ligand** identification: Pd pi-allyl chemistry as a "mutation mechanism.
AU **Klekota, Bryan; Miller, Benjamin L.**
CS Dep. Chem., Univ. Rochester, Rochester, NY 14627 USA
SO Abstracts of Papers American Chemical Society, (1999) Vol. 217, No. 1-2, pp. ORGN 173.
Meeting Info.: 217th National Meeting of the American Chemical Society

Anaheim, California, USA March 21-25, 1999 American Chemical Society . ISSN: 0065-7727.
DT Conference
LA English
CC Biochemical Methods - General *10050
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Minerals *10069
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Chemicals & Biochemicals
cyclopentene 1,4 diacetate: transesterification; palladium: pi-allyl chemistry; thrombin; trypsin
IT Methods & Equipment
ligand identification technique: identification method
IT Miscellaneous Descriptors
combinatorial chemistry **library**; mutation mutation; Meeting Abstract
RN 7440-05-3 (PALLADIUM)
9002-07-7 (TRYPSIN)
9002-04-4 (THROMBIN)

L19 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:42049 BIOSIS
DN PREV199800042049
TI Generation of novel DNA-binding compounds by selection and amplification from self-assembled combinatorial **libraries**.
AU **Klekota, Bryan**; Hammond, Mark H.; **Miller, Benjamin L.** **(1)**
CS (1) Dep. Chem., Univ. Rochester, Rochester, New York 14627 USA
SO Tetrahedron Letters, (Dec. 15, 1997) Vol. 38, No. 50, pp. 8639-8642. ISSN: 0040-4039.
DT Article
LA English
AB We describe a general method for the selection of compounds from self-assembled **libraries** which employs an immobilized receptor (i.e., an affinity reagent) to effect the selection. Using commercially available oligo d(AcntdotT) DNA-cellulose resin, a set of three stereoisomeric coordination complexes are identified as DNA binding compounds from an equilibrating, self-assembled **library** of 36 bis(salicylaldiminato)-zinc coordination complexes.
CC Biochemical Methods - General *10050
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Carbohydrates *10068
Biochemical Studies - Minerals *10069
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics
IT Chemicals & Biochemicals
bis(salicylaldazine)-zinc coordination complexes; DNA-binding compounds: generation; DNA-cellulose resin
IT Methods & Equipment
self-assembled combinatorial **libraries**: amplification, selection, synthetic method

L19 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:198282 BIOSIS
DN PREV199799497485
TI Self-assembled, self-amplifying combinatorial **libraries** as a new method for **ligand** discovery: Application to DNA-binding compounds.
AU **Klekota, Bryan**; Hammond, Mark H.; **Miller, Benjamin L.**
CS Dep. Chem., Univ. Rochester, Rochester, NY 14607 USA

SO Abstracts of Papers American Chemical Society, (1997) Vol. 213, No. 1-3, pp. ORGN 573.
Meeting Info.: 213th National Meeting of the American Chemical Society San Francisco, California, USA April 13-17, 1997
ISSN: 0065-7727.
DT Conference; Abstract
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Miscellaneous Descriptors
ANALYTICAL METHOD; CHEMISTRY; DNA-BINDING COMPOUNDS; IDENTIFICATION; **LIGAND** DISCOVERY; METHODOLOGY; SELF-ASSEMBLED COMBINATORIAL **LIBRARY** APPROACH; SYNTHESIS; SYNTHETIC METHOD

L19 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:422915 BIOSIS
DN PREV199598437215
TI An approach to the discovery of novel **ligands** for proteins involved in signal transduction.
AU Combs, Andrew P.; Kapoor, Tarun M.; Chen, James K.; **Miller, Benjamin L.**; Miyake, Hiroshi; Feng, Sibo; Yu, Hongtao; Snow, Lygia F.; Gelman, Michael A.; Schreiber, Stuart L.
CS HHMI, Dep. Chem., Harvard Univ., Cambridge, MA 02138 USA
SO Abstracts of Papers American Chemical Society, (1995) Vol. 210, No. 1-2, pp. ORGN 411.
Meeting Info.: 210th American Chemical Society National Meeting Chicago, Illinois, USA August 20-24, 1995
ISSN: 0065-7727.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
General Biology - Information, Documentation, Retrieval and Computer Applications *00530
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Studies *10502
Biophysics - Biocybernetics *10515
IT Major Concepts
Biochemistry and Molecular Biophysics; Information Studies; Models and Simulations (Computational Biology)
IT Miscellaneous Descriptors
COMPUTER MODELING; MEETING ABSTRACT; NMR; PEPTIDE **LIBRARY** SCREENING

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E MILLER BEN/AU
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E KLEKOTA B/AU
L22 5 S E4
L23 5 S L20,L21 AND L22
L24 236 S L20-L22
L25 11 S L24 AND LIGAND
L26 7 S L24 AND LIBRARY
L27 5 S L25 AND L26
L28 6 S L23,L27

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L29            7 S L25-L26 NOT L28
L30            4 S L29 NOT (SYNECHOC? OR PHOSPHIDE)/TI
L31           10 S L28,L30

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L31  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2000 ACS
AN   2000:129017  HCAPLUS
TI   Dynamic diversity in drug discovery: putting small-molecule evolution to
     work
AU   Karan, Charles; Miller, Benjamin L.
CS   Department of Chemistry, University of Rochester, Rochester, NY, 14627,
     USA
SO   Drug Discovery Today (2000), 5(2), 67-75
     CODEN: DDTOFS; ISSN: 1359-6446
PB   Elsevier Science Ltd.
DT   Journal
LA   English
CC   1 (Pharmacology)
AB   From oligonucleotides to orangutans, nature has found darwinian evolution
     to be the most efficient means of optimizing populations of organisms - or
     mols.  Recently, several research groups have begun adapting darwinian
     evolution to the identification of small mols. with specific properties.
     Although still at an early stage, this new field of "dynamic diversity"
     shows promise as a method for the identification of high-affinity
     ligands for biomols.

L31  ANSWER 2 OF 10  HCAPLUS  COPYRIGHT 2000 ACS
AN   1999:625541  HCAPLUS
DN   131:333540
TI   Selection of DNA-binding compounds via multistage molecular evolution
AU   Klekota, Bryan; Miller, Benjamin L.
CS   Department of Chemistry, University of Rochester, Rochester, NY, 14627,
     USA
SO   Tetrahedron (1999), 55(39), 11687-11697
     CODEN: TETRAB; ISSN: 0040-4020
PB   Elsevier Science Ltd.
DT   Journal
LA   English
CC   6-2 (General Biochemistry)
AB   Combinatorial libraries incorporating multiple equil. offer
```

opportunities to study mol. evolution, and are a novel method of identifying **ligands** for biol. receptors. We describe the construction and evaluation of a multi-equil. combinatorial **library**, in which structural diversity and structural mutation are accomplished via reversible imine formation and transition-metal complexation. We demonstrate that oligo d(A.cntdot.T)-cellulose resin can select subsets of this **library**, in accord with measured soln.-phase affinities.

ST DNA binding compd mol evolution combinatorial **library**

IT Evolution
(mol.; selection of DNA-binding compds. via multistage mol. evolution)

IT Combinatorial **library**
(selection of DNA-binding compds. via multistage mol. evolution)

IT DNA
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(selection of DNA-binding compds. via multistage mol. evolution)

IT 156-87-6 617-89-0, 2-Aminomethylfuran 1583-88-6, 4-Fluorophenethylamine 2706-56-1, 2-Aminoethylpyridine 3117-65-5 5332-73-0, 3-Methoxypropylamine 7059-24-7, Chromomycin A3 14167-22-7 51387-90-7 74733-75-8
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(selection of DNA-binding compds. via multistage mol. evolution)

L31 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:526036 HCAPLUS
DN 131:266426
TI Dynamic diversity and small-molecule evolution: a new paradigm for **ligand** identification
AU **Klekota, Bryan; Miller, Benjamin L.**
CS Department of Chemistry, University of Rochester, Rochester, NY, 14627, USA
SO Trends Biotechnol. (1999), 17(5), 205-209
CODEN: TRBIDM; ISSN: 0167-7799
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review with 21 refs. A longstanding goal of org., medicinal and bioorg. chemists has been the discovery of efficient methods for designing or identifying biol. active compds. Recently, several groups have reported using the directed evolution of combinatorial **libraries** as a new method of identifying compds. capable of binding tightly to a target mol. Although significant development remains to be done, the initial results suggest that dynamic diversity and assocd. selection methods will prove to be valuable addns. to the drug-discovery process.

ST review receptor **ligand** identification drug discovery; combinatorial **library** receptor **ligand** identification review

IT Combinatorial **library**
Drug screening
(dynamic diversity and small-mol. evolution and new paradigm for receptor **ligand** identification for use with combinatorial **libraries** in relation to drug discovery)

IT **Ligands**
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(dynamic diversity and small-mol. evolution and new paradigm for receptor **ligand** identification for use with combinatorial **libraries** in relation to drug discovery)

L31 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:145606 HCAPLUS
TI Evolving combinatorial **libraries** as a novel method for **ligand** identification: Pd .pi.-allyl chemistry as a "mutation

mechanism"
AU **Klekota, Bryan; Miller, Benjamin L.**
CS Department of Chemistry, University of Rochester, Rochester, NY, 14627, USA
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), ORGN-173 Publisher: American Chemical Society, Washington, D. C.
CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB **Libraries** generated under equilibrating conditions in the presence of a receptor show promise as a new means of **ligand** identification. We will describe the results of a **library** selection and amplification scheme in which the Pd-catalyzed transesterification of cyclopentene 1,4 diacetate is used, under equilibrating conditions, to generate **ligands** for trypsin and thrombin. [Equation Omitted].

L31 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:790866 HCAPLUS
DN 128:137688
TI Generation of novel DNA-binding compounds by selection and amplification from self-assembled combinatorial libraries
AU **Klekota, Bryan;** Hammond, Mark H.; **Miller, Benjamin L.**
CS Department of Chemistry, University of Rochester, Rochester, NY, 14627, USA
SO Tetrahedron Lett. (1997), 38(50), 8639-8642
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
CC 6-2 (General Biochemistry)
Section cross-reference(s): 25
AB We describe a general method for the selection of compds. from self-assembled libraries which employs an immobilized receptor (i.e., an affinity reagent) to effect the selection. Using com. available oligo d(A.cntdot.T) DNA-cellulose resin, a set of three stereoisomeric coordination complexes are identified as DNA binding compds. from an equilibrating, self-assembled library of 36 bis(salicylaldiminato)-zinc coordination complexes.
ST bissalicylaldiminatozinc DNA binding compd combinatorial library
IT Combinatorial library
DNA-binding structure-activity relationship
Molecular association
(generation of novel DNA-binding compds. by selection and amplification from self-assembled combinatorial libraries)
IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(generation of novel DNA-binding compds. by selection and amplification from self-assembled combinatorial libraries)
IT 24939-09-1, Poly d(A.cntdot.T)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(generation of novel DNA-binding compds. by selection and amplification from self-assembled combinatorial libraries)
IT 112360-49-3P 201986-26-7P 201986-27-8P 201986-28-9P 201986-29-0P
201986-30-3P 201986-31-4P 201986-32-5P 201986-33-6P 201986-34-7P
201986-35-8P 201986-36-9P 201986-37-0P 201986-38-1P 201986-39-2P
201986-40-5P 201986-41-6P 201986-42-7P 201986-43-8P 201986-44-9P
201986-45-0P 202074-91-7P 202074-92-8P 202074-93-9P 202074-94-0P
202074-95-1P 202074-96-2P 202074-97-3P 202074-98-4P 202074-99-5P
202075-00-1P 202075-01-2P 202075-02-3P 202075-03-4P 202217-38-7P
202217-39-8P
RL: BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(generation of novel DNA-binding compds. by selection and amplification from self-assembled combinatorial libraries)

L31 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:162835 HCAPLUS
TI Self-assembled, self-amplifying combinatorial **libraries** as a new method for **ligand** discovery: Application to DNA-binding compounds.
AU **Klekota, Bryan**; Hammond, Mark H.; **Miller, Benjamin L.**
CS Department Chemistry, University Rochester, Rochester, NY, 14607, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), ORGN-573 Publisher: American Chemical Society, Washington, D. C. CODEN: 64AOAA
DT Conference; Meeting Abstract
LA English
AB Processes such as the polymerase chain reaction and in vitro selection of RNA aptamers have demonstrated the power of selection and amplification methods for the identification of biopolymeric **ligands** to receptors. As part of an effort to study analogous selection and amplification processes for nonbiopolymeric materials, we have developed a self-assembled combinatorial **library** approach to **ligand** synthesis that employs a solid-supported affinity reagent to select tight-binding compds. from an equilibrating mixt. of coordination compds. Results of the application of this method to the identification of novel DNA-binding compds. will be presented.

L31 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:925025 HCAPLUS
TI An approach to the discovery of novel **ligands** for proteins involved in signal transduction
AU Combs, Andrew P.; Kapoor, Tarun M.; Chen, James K.; **Miller, Benjamin L.**; Miyake, Hiroshi; Feng, Sibo; Yu, Hongtao; Snow, Lygia F.; Gelman, Michael A.; Schreiber, Stuart L.
CS HHMI, Harvard University, Cambridge, MA, 02138, USA
SO Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, ORGN-411 Publisher: American Chemical Society, Washington, D. C.
CODEN: 61XGAC
DT Conference; Meeting Abstract
LA English
AB We screened a biased combinatorial peptide **library** and identified unique proline-rich peptides that bind SH3 domains of various signaling proteins. Multidimensional NMR anal. of these receptor-**ligand** complexes revealed two unique binding modes for the .alpha.-helical peptides to the SH3 domains. Extension of these studies to the discovery of novel non-peptidic **ligands** via computer modeling, encoded combinatorial synthesis and enzymic on-bead assays will be discussed. These studies highlight our four stage approach to **ligand** discovery: 1) combinatorial peptide **library** screening 2) identification of **ligands** and multidimensional NMR anal. of receptor-**ligand** complexes, 3) computer modeling directed toward novel **library** design, 4) combinatorial synthesis of non-peptidic **libraries** and iteration of steps 2 and 3.

L31 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:303405 HCAPLUS
DN 122:208556
TI Identification, activity, and structural studies of peptides incorporating the phorbol ester-binding domain of protein kinase C
AU Wender, Paul A.; Irie, Kazuhiro; **Miller, Benjamin L.**
CS Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1995), 92(1), 239-43
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 7-5 (Enzymes)
AB The identification, synthesis, **ligand**-binding anal., cofactor requirements, and preliminary NMR evaluation of 2 subdomains [peptide B

(residues 36-87) and peptide C (residues 101-151)] of the regulatory domain of protein kinase C isoenzyme .gamma. (PKC-.gamma.) are described. Peptides B and C bound [3H]phorbol 12,13-dibutyrate with good affinity (Kd = 6.4 .mu.M and 414 nM, resp.) in the presence of phosphatidylserine. For comparison, the binding affinity of [3H]phorbol 12,13-dibutyrate for PKC was found to be 2.6 nM. Like PKC itself, these peptides also recognized other PKC activators, including dioctanoylglycerol and teleocidin B-4, and exhibited an ability to differentiate phorbol ester from its C-4 epimer. NMR studies of PKC subdomains were also described, indicating that both peptides B and C are well behaved in soln. and do not exhibit any concn.-dependent changes. Finally, these studies revealed that peptide B became conformationally ordered only in the presence of phospholipid, suggesting that the regulatory domain of PKC itself may be organized for activation only when assocd. with the lipid bilayer, where its activator (diacylglycerol) is encountered.

ST protein kinase C domain structure activity; phorbol ester domain protein kinase C

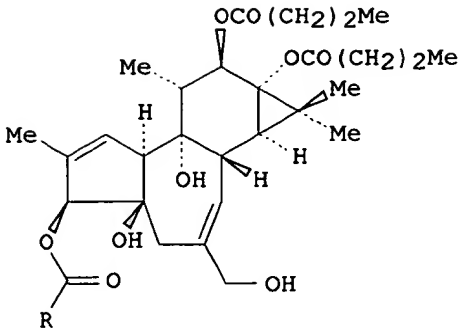
IT Phosphatidylserines
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(studies of peptides incorporating the phorbol ester-binding domain of protein kinase C)

IT 141436-78-4, Protein kinase C
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(isoenzyme .gamma., phorbol ester-binding domain; studies of peptides incorporating the phorbol ester-binding domain of protein kinase C)

IT 11032-05-6, Teleocidin B-4 37558-16-0, Phorbol 12,13-dibutyrate 60514-48-9
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(studies of peptides incorporating the phorbol ester-binding domain of protein kinase C)

IT 161938-23-4P 161938-24-5P
RL: BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(studies of peptides incorporating the phorbol ester-binding domain of protein kinase C)

L31 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:603646 HCAPLUS
DN 119:203646
TI Synthesis and binding of photoaffinity **ligand** candidates for protein kinase C
AU Wender, Paul A.; Irie, Kazuhiro; **Miller, Benjamin L.**
CS Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA
SO J. Org. Chem. (1993), 58(16), 4179-81
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
CC 30-20 (Terpenes and Terpenoids)
OS CASREACT 119:203646
GI



I

AB The authors' observation that protein kinase C binding is retained by phorbol esters modified at the C(3) position has led to the design of a new class of photoaffinity **ligand** candidates. The first members of this class, esters I (R = CHN2) and I (R = 2-O2N-5-N3C6H3)were synthesized from phorbol and found to bind to protein kinase C with high affinity. The soln. photochem. of I (R = CHN2) leads predominantly to insertion products, as required for its use as a protein kinase C receptor probe.

ST protein kinase C photoaffinity **ligand**; phorbol ester kinase photoaffinity substrate

IT Affinity
(photo-, **ligands** for protein kinase C, phorbol esters as)

IT 17673-25-5, Phorbol
RL: RCT (Reactant)
(acylation of, with butyric anhydride)

IT 141436-78-4, Protein kinase C
RL: RCT (Reactant)
(photoaffinity **ligands** for, prepn. of)

IT 150537-61-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation of, with azidonitrobenzoic acid or N-protected glycine)

IT 150537-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT 150537-71-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and regioselective deacylation of)

IT 150537-70-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and stereoselective redn. of)

IT 150537-62-5P 150537-63-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as photoaffinity labeled for protein kinase C)

IT 150577-47-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, stereoselectivity in)

IT 115792-14-8P 150537-64-7P 150537-65-8P 150537-66-9P 150537-67-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, via photolysis of phorbol ester)

IT 150537-69-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., N-deprotection, and diazotization of)

L31 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN 1989:515502 HCAPLUS
DN 111:115502
TI Isodicyclopentadienes and related molecules. 48. Stereochemically uniform mode of iron carbonyl complexation to spirocyclic isodicyclopentadienes
AU Paquette, Leo A.; O'Doherty, George A.; **Miller, Benjamin L.**;

Rogers, Robin D.; Rheingold, Arnold L.; Geib, Steven L.
CS Evans Chem. Lab., Ohio State Univ., Columbus, OH, 43210, USA
SO Organometallics (1989), 8(9), 2167-72
CODEN: ORGND7; ISSN: 0276-7333
DT Journal
LA English
CC 29-12 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 75
OS CASREACT 111:115502
GI For diagram(s), see printed CA Issue.
AB The **ligands** I derived by suitable spiroalkylation of isodicyclopentadiene were reacted with various iron carbonyl reagents in order to assess .pi.-facial stereoselectivity and other reactivity differences. In contrast to the behavior of these dienes in Diels-Alder reactions, complexation occurred only above-plane. The less strained spiro[4.4]nonadiene I (n = 4) reacts with Fe2(CO)9 to form the .eta.4-iron complex, the 3-dimensional features of which were established by crystallog. anal. The results of heating I (n = 4) with (BDA)Fe(CO)3 (BDA = benzylideneacetone) in benzene were bond fission and formation of the .sigma.-allyl .pi.-isodicyclopentadienyl complex II. The latter substance could not be made to undergo carbonyl insertion. For I (n = 2), heating with (BDA)Fe(CO)3 led directly to the .sigma.-acyl system III for which x-ray data were also obtained. Use of Fe2(CO)9 delivered a mixt. of III and the fulvene complex IV. The uniform mode of iron carbonyl complexation throughout this series is attributed to steric approach control.
ST spirocyclic isodicyclopentadiene complexation iron carbonyl; crystal mol structure isodicyclopentadieneiron complex
IT Crystal structure
Molecular structure
(of isodicyclopentadiene iron complexes)
IT 1184-78-7, Trimethylamine oxide
RL: RCT (Reactant)
(cyclopentane ring opening-cyclization by, of spirocyclic isodicyclopentadiene iron complex)
IT 121935-65-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and crystal structure of)
IT 121935-63-5P 121935-64-6P 121935-66-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 121962-53-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., crystal structure, and cyclopentane ring opening-cyclization of)
IT 81897-89-4
RL: RCT (Reactant)
(reaction of, with benzalidene acetone iron tricarbonate complex)
IT 81897-93-0
RL: RCT (Reactant)
(reaction of, with diiron nonacarbonyl)
IT 15321-51-4, Diiron nonacarbonyl 38333-35-6
RL: RCT (Reactant)
(reaction of, with spirocyclic isodicyclopentadienes)

=> d his l32-

FILE 'MEDLINE' ENTERED AT 09:51:36 ON 27 MAR 2000
E MILLER B/AU
L32 584 S E3,E16
E KLEKOTA B/AU
L33 1 S E3
L34 584 S L32,L33
L35 4 S L34 AND LIGAND

```
     FILE 'WPIDS' ENTERED AT 09:52:41 ON 27 MAR 2000
                E MILLER B/AU
L36           89 S E3,E14
                E KLEKOTA B/AU
L37            0 S L36 AND LIGAND
L38            0 S L36 AND LIBRARY
L39           16 S L36 AND ?METAL?

     FILE 'HCAPLUS' ENTERED AT 09:57:13 ON 27 MAR 2000
L40       250779 S LIGAND
L41       259492 S ?LIGAND?
L42         2118 S L41 AND LIBRARY
L43         1212 S L42 AND (DNA? OR ?DEOXYRIBONUCLEIC? OR ?RIBONUCLEIC? OR NUCLE
L44           12 S L43 AND TRANSITION
L45           12 S L42 AND TRANSITION METAL
L46         1670 S L42 AND PY<=1998
L47          430 S L42 AND PRY<=1998
L48          410 S L42 AND PRY.B<=1998
L49          374 S L42 AND AY<=1998
L50          370 S L42 AND AY.B<=1998
L51         1809 S L46-L50
L52           11 S L51 AND L45
L53           11 S L52 NOT L31
L54           11 S L45 NOT L31
L55            7 S L51 AND NONBIO?
L56            0 S L51 AND NON BIO?
L57          507 S L51 AND ?POLY?
L58            7 S L51 AND POLY?/SC,SX
L59            2 S L58 AND (UNNATURAL OR ORGANOMETALLIC)
L60          373 S L57 AND L43
L61            0 S L60 AND INTERCALAT?
L62            1 S L60 AND GROOVE
L63           18 S L60 AND CONFORMATION
L64            7 S P/DT AND L63
L65            6 S L64 AND (TARGET? OR SCREEN? OR PROBE?)
L66            5 S L65 NOT PHAGE/TI
L67            8 S L62,L66,L59
L68           73 S L51 AND REVERS?
L69            0 S L68 AND GROOV?
L70            0 S L68 AND ?BIOPOLYM?
L71            0 S L70 AND L57
L72            3 S L68 AND (TEMPLATE OR SELEX OR NATURAL)/TI
L73          198 S SELEX AND L41
L74           53 S L73 AND L51
L75          151 S SYSTEM? (L) EVOL? (L) EXPONENT? (L) ENRICH?
L76          141 S L75 AND L41
L77           39 S L76 AND L42
L78           36 S L77 AND L51
L79           60 S L74,L78,L72,L67 NOT L31

=> d bib abs tot 179


L79  ANSWER 1 OF 60  HCAPLUS  COPYRIGHT 2000 ACS
AN   2000:140562  HCAPLUS
TI   Parallel systematic evolution of ligands by
     exponential enrichment (parallel SELEX).
IN   Eaton, Bruce; Gold, Larry
PA   NeXstar Pharmaceuticals, Inc., USA
SO   U.S., 39 pp., Cont.-in-part of U.S. Ser. No. 309,245, abandoned.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 81
     PATENT NO.       KIND  DATE           APPLICATION NO.  DATE
```

PI	US 6030776	A	20000229	US 1997-793398	19970224 <--
	US 5475096	A	19951212	US 1991-714131	19910610 <--
	EP 786469	A2	19970730	EP 1997-200035	19910610 <--
	EP 786469	A3	19970806		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	IL 112141	A1	19980405	IL 1991-112141	19910611 <--
	US 5723289	A	19980303	US 1994-309245	19940920 <--
	WO 9609316	A1	19960328	WO 1995-US11982	19950919 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PRAI	US 1990-536428	19900611 <--			
	US 1991-714131	19910610 <--			
	US 1994-309245	19940920 <--			
	WO 1995-US11982	19950919 <--			
	EP 1991-912753	19910610 <--			
	IL 1991-98456	19910611 <--			

AB This invention discloses a method for coevolving products from two or more reactants, along with the nucleic acid that can facilitate the reaction for making the products. The invention further discloses the products and facilitating nucleic acids produced by said method. A method for identifying a product from a product **library**, wherein said product is selected for its ability to perform a preselected function on a target, the method comprising (1) prepg. a nucleic acid-reactant test mixt. composed of nucleic acids each having a region of randomized sequence and each being assocd. with a first reactant, (2) reacting the test mixt. with a free reactant to form a **library** of products, wherein the reaction is facilitated by the nucleic acid assocd. with the first reactant, and (3) partitioning members of the product **library** based on their relative ability to perform their preselected function on a target, whereby said products can be identified. Thus, parallel **SELEX** was carried out involving reaction of 5'-guanosine monophosphorothioate attached to a random RNA 76-mer mixt. (initially approx. 5 .times. 1013 different mols.) with bromoacetylated bradykinin. After 12 rounds, an RNA conjugate was found which showed a 6700-fold increase in kcat/Km for the coupling reaction.

L79 ANSWER 2 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:68592 HCAPLUS
DN 132:105019
TI Synthesis and identification of bivalent binding RNA molecules to G protein-coupled receptors
IN Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PI	WO 2000004184	A1	20000127	WO 1999-US14853	19990630 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1998-118525	19980717 <--			

AB Methods for identifying and prepg. bivalent binding mols. to 7 transmembrane domain contg. G protein-coupled receptors is described. The methods are based on the **SELEX** method (**Systematic Evolution** of **Ligands** by **EXponential enrichment**) for generating high affinity nucleic acid **ligands**, termed aptamers. It combines two or more binding domains to two or more different epitopes of the same 7 transmembrane G protein-coupled receptor. The method was exemplified by screening in the random RNA **library** for binding mols. to either ECL1 (extracellular loop 1) or ECL2 of neurokinin receptor NK1R using peptide affinity columns. The bivalent **ligands**, derived from two ECL1- and ECL1-binding RNA **libraries** by linking them through overlap-extension PCR reaction, can be **enriched** after cycles of **SELEX** process to generate double-stranded DNA templates for their future synthesis . These bivalent binding mols. may be useful as therapeutic and diagnostic agents.

L79 ANSWER 3 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:691249 HCAPLUS
DN 131:318547
TI Method of isolating oligonucleotide **ligands** specific for protein targets by **SELEX** using a minimum number of rounds
IN Li, Weihua
PA Bioage Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9954506	A1	19991028	WO 1999-US8561	19990419 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-82405 19980420 <--
AB A method of rapidly identifying oligonucleotide **ligands** for target proteins (aptamers) without the multiple rounds of selection and amplification normally found in **SELEX** is described. The method uses an immobilized **library** of oligonucleotides contg. a randomized central sequence and common termini. The **library** is immobilized on particulate carriers such as resin beads and it is screened with the target protein bound to smaller magnetic particles or labeled with a fluorescent probe. Aptamers can then be screened for by fluorescence activated sorting or magnetic sepn. Use of the method to identify aptamers for erythropoietin is demonstrated.

L79 ANSWER 4 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:577054 HCAPLUS
DN 131:181959
TI Mass spectrometric methods for biomolecular **screening**
IN Crooke, Stanley T.; Griffey, Richard; Hofstadler, Steve
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9945150 A1 19990910 WO 1999-US4560 19990302 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9929773 A1 19990920 AU 1999-29773 19990302 <--
PRAI US 1998-PV76534 19980302 <--
US 1998-76206 19980512 <--
US 1998-76534 19980302 <--
WO 1999-US4560 19990302
AB The present invention provides methods for the detn. of the structure of biomol. **targets**, as well as the site and nature of the interaction between **ligands** and biomol. **targets**. The present invention also provides methods for the detn. of the relative affinity of a **ligand** for the biomol. **target** it interacts with. Also provided are methods for **screening** **ligand** or combinatorial **libraries** of compds. against one or more than one biol. **target** mols. The methods of the invention also allow detn. of the relative binding affinity of combinatorial and other compds. for a biomol. **target**. The present invention further provides methods for the use of mass modifying tags for **screening** multiple biomol. **targets**. In a preferred embodiment, **ligands** which have great specificity and affinity for mol. interaction sites on biomols., esp. RNA can be identified. In preferred embodiments, such identification can be made simultaneously with **libraries** of **ligands**.

L79 ANSWER 5 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:451485 HCAPLUS
DN 131:83961
TI Method for preparing biomacromolecule-binding **oligoligands** and their use for affinity chromatography, biomacromolecule detection and therapy
IN Gasch, Alexander; Friday, Douglas; Berghof, Kornelia; Mueller-Kuhrt, Lutz
PA BioteCon Gesellschaft fuer Biotechnologische Entwicklung und Consulting m.b., Germany
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19800899	A1	19990715	DE 1998-19800899	19980113 <--
WO 9936430	A1	19990722	WO 1999-EP120	19990112 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9926163 A1 19990802 AU 1999-26163 19990112 <--
PRAI DE 1998-19800899 19980113 <--
WO 1999-EP120 19990112
AB The title method for prepg. **oligoligands** which bind to a biol. macromol. and/or which has a desired biol. activity comprises (1) selection of **ligands** which bind to a monomeric or oligomeric monomer (e.g., an amino acid, dipeptide, or tripeptide); (2)selection of more **ligands** as in step 1; (3) combining and linking of the

selected **ligands** to prep. a combinatorial **library** of **oligoligands**; (4) screening of the **library** for binding to a desired macromol. or for a desired biol. activity; and (5) isolation of the **oligoligand**(s) with desired properties. Use of the **oligoligands** in affinity chromatog., for detection of biol. macromols., and for therapy (e.g, antibacterial, antiviral, or antitumor use) is disclosed.

L79 ANSWER 6 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:405121 HCAPLUS
DN 131:54725
TI Homogeneous detection of a **target** through **nucleic** acid **ligand-ligand** beacon interaction
IN Jayasena, Sumedha; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9931276	A1	19990624	WO 1998-US26599	19981215	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 5989823	A	19991123	US 1998-157206	19980918	<--

PRAI US 1997-68135 19971215 <--
US 1998-157206 19980918 <--

AB A homogeneous assay that utilizes mol. beacons as the reporter and **nucleic** acid **ligands** as the sensor is described. This assay, called the **ligand** beacon assay, is for the detection of **target** mols. in a test mixt. The concept of the **ligand** beacon assay was tested using several proteins to which high affinity and specific **nucleic** acid **ligands** are available. The assay specifically detects the mol. **target** that binds the **nucleic** acid **ligand** with high affinity and specificity. The range of the assay is dictated by the concn. of the **nucleic** acid **ligand/ligand** beacon pair used in the assay. **Target** proteins were detected in buffer as well as in plasma, expanding its applicability to clin. use. This is a simple to use and fast assay format with the potential for automation for high throughput **screening** applications.

L79 ANSWER 7 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:405112 HCAPLUS
DN 131:56155
TI Methods for the simultaneous identification of novel biological **targets** and lead structures for drug development using combinatorial **libraries** and **probes**
IN Heefner, Donald L.; Zepp, Charles M.; Gao, Yun; Jones, Steven W.
PA Sepracor Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9931267	A1	19990624	WO 1998-US26894	19981218	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,					

DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9919256 A1 19990705 AU 1999-19256 19981218 <--
PRAI US 1997-68035 19971218 <--
US 1997-PV68035 19971218 <--
WO 1998-US26894 19981218 <--

AB The combinatorial **screening** assays and detection methods of the present invention encompass highly diversified **libraries** of compds. which act as fingerprints to allow for the identification of specific mol. differences existing between biol. samples. The combinatorial **screening** assay and detection methods of the present invention utilize highly diversified **libraries** of compds. to interrogate and characterize complex mixts. in order to identify specific mol. differences existing between biol. samples, which may serve as **targets** for diagnosis of development of therapeutics. The invention is base, in part, on the design of sensitive, rapid, homogeneous assay systems that permit the evaluation, interrogation, and characterization of samples using complex, highly diversified **libraries** of mol. **probes**. The ability to run the high throughput assays in a homogeneous format increases sensitivity of **screening**. In addn., the homogeneous format allows the mols. which interact to maintain their native or active **conformations**. Moreover, the homogeneous assay systems of the invention utilize robust detection systems that do not require sepn. steps for detection of reaction products. The assays of the invention can be used for diagnostics, drug **screening** and discovery, **target**-driven discover, and in the field of proteomics and genomics for the identification of disease markers and drug **targets**.

L79 ANSWER 8 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:359686 HCAPLUS
DN 131:14830
TI Improved **SELEX** procedure and an anti-CD4 aptamer
IN James, William Siward; Barclay, Alan Neil; Kraus, Elmar
PA Medical Research Council, UK
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9927133	A1	19990603	WO 1998-GB3544	19981126 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9912520 A1 19990615 AU 1999-12520 19981126 <--
PRAI GB 1997-25024 19971126 <--
US 1998-78221 19980316 <--
US 1998-PV78221 19980316 <--
WO 1998-GB3544 19981126 <--

AB The invention provides an improved **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) method for isolating a nucleic acid capable of binding to a target from a **library** of single-stranded nucleic acid

members, by selecting **library** members according to their dissocn. kinetics. A problem which stems from the power of **SELEX** to **enrich** for specific binding aptamers among up to 1018 mols. is that it is very often the case that the 10-20 cycles of selection needed to achieve this require usually around 8 wk to complete. The invention makes use of the rate of dissocn. of mols. from the target, rather than their rate of assocn. with it, to select suitable aptamers. This permits the more rapid selection of mols. having a high affinity for the target than the methods of the prior art. The improved **SELEX** procedure is used to select 2'-fluoro modified RNA aptamers that inhibit a mixed lymphocytic reaction by their affinity for CD4.

L79 ANSWER 9 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:166720 HCAPLUS
DN 130:205971
TI RNA transcriptional regulators and their identification and uses
IN Jarrell, Kevin A.; Saha, Shamol; Ptashne, Mark
PA President and Fellows of Harvard College, USA; Trustees of Boston University
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9910487	A2	19990304	WO 1998-US17691	19980826 <--
	WO 9910487	A3	19990701		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9891212	A1	19990316	AU 1998-91212	19980826 <--
PRAI	US 1997-56857		19970827 <--		
	WO 1998-US17691		19980826 <--		

AB The present invention provides RNA mols. that regulate transcription. Specifically, the invention provides RNAs that, when recruited to a site operatively linked to a promoter, increase or decrease the rate or extent of transcription from that promoter. Methods of isolating such RNAs, termed "riboregulators", are provided, based on a modified Wickens/Fields **system** (Proc. Natl. Acad. Sci. USA 93:8496, 1996) and the **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) **system** developed by Larry Gold and colleagues. The riboregulators have stem-loop structures similar to those of Tar or Keene RNA, and a consensus sequence of 5'-ugc(g>u>a)gg(u>a>c)(u>acg)(c>a)(g>a>u)-3'.

L79 ANSWER 10 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:69919 HCAPLUS
DN 130:134950
TI **Systematic evolution** of **ligands** by **exponential enrichment**: tissue **SELEX**
IN Jensen, Kirk; Chen, Hang; Morris, Kevin N.; Stephens, Andrew; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 61 pp., Cont.-in-part of U.S. 5,475,096.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5864026	A	19990126	US 1995-437667	19950503 <--

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     US 5475096          A    19951212       US 1991-714131   19910610 <--
     EP 786469           A2   19970730       EP 1997-200035   19910610 <--
     EP 786469           A3   19970806
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     IL 112141           A1   19980405       IL 1991-112141   19910611 <--
     US 5496938          A    19960305       US 1992-964624   19921021 <--
     CA 2219807          AA   19961107       CA 1996-2219807  19960501 <--
     WO 9634875          A1   19961107       WO 1996-US6060   19960501 <--
        W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
            ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,
            LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
            IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI
     AU 9656707          A1   19961121       AU 1996-56707    19960501 <--
     EP 823914           A1   19980218       EP 1996-913880   19960501 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
PRAI US 1990-536428    19900611  <--
     US 1991-714131    19910610  <--
     US 1992-964624    19921021  <--
     EP 1991-912753    19910610  <--
     IL 1991-98456     19910611  <--
     US 1995-433585    19950503  <--
     US 1995-434001    19950503  <--
     US 1995-434425    19950503  <--
     US 1995-437667    19950503  <--
     WO 1996-US6060    19960501  <--
AB   This invention discloses high-affinity oligonucleotide ligands
     to complex tissue targets, specifically nucleic acid ligands
     having the ability to bind to complex tissue targets, and the methods for
     obtaining such ligands.  Tissue targets comprise cells,
     subcellular components, aggregates or cells, collections of cells, and
     higher ordered structures.  Specifically, nucleic acid ligands
     to red blood cells ghosts, glioblastomas, and lymphomas are described.

L79  ANSWER 11 OF 60  HCAPLUS  COPYRIGHT 2000 ACS
AN   1999:64919  HCAPLUS
DN   130:120449
TI   A method of screening for genes by expression using in vitro
     transcription/translation systems in microparticulate emulsions
IN   Griffiths, Andrew; Tawfik, Dan
PA   Medical Research Council, UK
SO   PCT Int. Appl., 101 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
     ---------------     ----  --------       ---------------  --------
PI   WO 9902671          A1    19990121       WO 1998-GB1889   19980629 <--
        W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
            KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
            NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
            UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
            CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9881231          A1    19990208       AU 1998-81231    19980629 <--
PRAI GB 1997-14300     19970707  <--
     GB 1998-6393      19980325  <--
     WO 1998-GB1889    19980629  <--
AB   A method for selecting genes or for in vitro evolution of cloned sequences
     using microencapsulated transcription/translation systems is described.  A
     soln. contg. an RNA polymerase and components of an in vitro translation
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system and DNA is emulsified in oil to give microparticles contg. a few (.apprx.10) DNA fragments per microparticle. After allowing gene expression the emulsion is broken. This allows the transcription/translation complexes to re-enter the aq. phase where they can be screened, e.g. by binding to a specific **ligand**. The breaking of the emulsion does not require the use of detergents or other reagents that could disrupt the complexes meaning that the nucleic can be obtained assocd. with its gene product. The method is demonstrated by achieving coupled transcription and translation of the Escherichia coli folA (dihydrofolate reductase) gene using T7 polymerase and a com. S30 ext. The ability of the method to select for a given activity is demonstrated by reconstruction expts. selecting genes for DNA methylases that are present at 0.1% of total DNA. Enrichment of 500-fold was clearly visible after a single round of selection for restriction enzyme-resistant DNA. Enzyme assays and other prior art anal. methods that can be used in screening and selection of mutants are described.

L79 ANSWER 12 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:45047 HCAPLUS
DN 130:91264
TI Parallel **SELEX** allowing for asymmetrical reactions in combinatorial chemistry
IN Eaton, Bruce; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 51 pp., Cont.-in-part of U.S. 5,723,289.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5858660	A	19990112	US 1996-618700	19960320 <--
	US 5723289	A	19980303	US 1994-309245	19940920 <--
PRAI	US 1994-309245	19940920 <--			
	US 1990-536428	19900611 <--			
	US 1991-714131	19910610 <--			

AB This invention discloses a method for parallel **SELEX** (**Systematic Evolution** of **Ligands** by **Exponential enrichment**), consisting of prepg. a nucleic acid test mixt., coupling each nucleic acid to a small org. mol., forming a product **library** via bond formation of the attached org. mols. with free reactant(s) catalyzed by their attached nucleic acids, and selecting desired products, both for identification and for amplification of their catalytic nucleic acids. In this process, a large nucleic acid test mixt. is provided with each nucleic acid linked to a chem. reactant, premised on the assumption that in the **library** there will be nucleic acids capable of mediating a reaction between their own attached reactants and some other free reactants. Sepg. the desired products, then, allows for **enrichment** of their attached catalytic nucleic acids. Parallel **SELEX** can include the formation of product **libraries** using asym. reactions. Unlike conventional combinatorial chem. approaches, the reactions can be included with no knowledge of the stereochem. outcome. Generic examples using the parallel **SELEX** method are given.

L79 ANSWER 13 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:25972 HCAPLUS
DN 130:92475
TI Use of nucleic acid **ligands** in flow cytometry
IN Davis, Ken; Jayasena, Sumedha; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 16 pp., Cont.-in-part of U.S. 5,496,938.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5853984	A	19981229	US 1995-479729	19950607 <--
	US 5475096	A	19951212	US 1991-714131	19910610 <--
	EP 786469	A2	19970730	EP 1997-200035	19910610 <--
	EP 786469	A3	19970806		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	IL 112141	A1	19980405	IL 1991-112141	19910611 <--
	US 5496938	A	19960305	US 1992-964624	19921021 <--
	US 5472841	A	19951205	US 1994-199507	19940222 <--
	US 5683867	A	19971104	US 1994-234997	19940428 <--
	WO 9641019	A1	19961219	WO 1996-US8089	19960530 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
	AU 9661470	A1	19961230	AU 1996-61470	19960530 <--
	EP 832299	A1	19980401	EP 1996-919017	19960530 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI	US 1990-536428	19900611 <--
	US 1991-714131	19910610 <--
	US 1992-964624	19921021 <--
	US 1994-199507	19940222 <--
	US 1994-234997	19940428 <--
	EP 1991-912753	19910610 <--
	IL 1991-98456	19910611 <--
	US 1993-117991	19930908 <--
	US 1993-123935	19930917 <--
	US 1994-234797	19940428 <--
	US 1995-479729	19950607 <--
	WO 1996-US8089	19960530 <--

AB This invention describes methods for using nucleic acid **ligands** in flow cytometry applications. A nucleic acid **ligand** is a non-naturally occurring nucleic acid having a specific binding affinity for a target. A nucleic acid **ligand** can be directed to any target in any format that is suitable for use in flow cytometry. In a preferred embodiment, the nucleic acid **ligands** bind cell surface proteins with high affinity and specificity. In another embodiment, the nucleic acid **ligands** bind intracellular proteins. In yet another embodiment, the nucleic acid **ligands** bind to targets in a substance which has been coated on a solid support, such as a bead. The method utilized here for identifying and prepg. said nucleic acid **ligands** is called **SELEX**, an acronym for **Systematic Evolution** of **Ligands** by **Exponential enrichment**. The invention includes high-affinity nucleic acid **ligands** having attached one or more fluorophore mols. which may be employed in flow cytometric methodologies.

L79 ANSWER 14 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:816043 HCAPLUS
DN 130:77053
TI High-affinity **oligonucleotide ligands** to vascular endothelial growth factor (VEGF)
IN Janjic, Nebojsa; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 64 pp., Cont.-in-part of U.S. 5,475,096.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5849479	A	19981215	US 1994-233012	19940425 <--

PI US 5475096 A 19951212 US 1991-714131 19910610 <--
EP 786469 A2 19970730 EP 1997-200035 19910610 <--
EP 786469 A3 19970806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
IL 112141 A1 19980405 IL 1991-112141 19910611 <--
US 5496938 A 19960305 US 1992-964624 19921021 <--
CA 2169536 AA 19950316 CA 1994-2169536 19940908 <--
WO 9507364 A1 19950316 WO 1994-US10306 19940908 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9476865 A1 19950327 AU 1994-76865 19940908 <--
AU 692469 B2 19980611
EP 724647 A1 19960807 EP 1994-927409 19940908 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 09502354 T2 19970311 JP 1994-508834 19940908 <--
US 5811533 A 19980922 US 1995-447169 19950519 <--
US 5789163 A 19980804 US 1995-487425 19950607 <--
PRAI US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-964624 19921021 <--
EP 1991-912753 19910610 <--
IL 1991-98456 19910611 <--
US 1993-117991 19930908 <--
US 1993-134028 19931007 <--
US 1994-199507 19940222 <--
US 1994-205515 19940303 <--
US 1994-233012 19940425 <--
US 1994-234997 19940428 <--
WO 1994-US10306 19940908 <--
AB This invention describes the isolation and characterization of binding properties of a set of high-affinity RNA **ligands** to vascular endothelial growth factor (VEGF). These **ligands** were selected from an initial pool of about 1014 RNA mols. randomized at thirty contiguous positions. The evolved RNA **ligands** bind VEGF with affinities in the low nanomolar range. Also described are modified RNA **ligands** to VEGF. Such modified RNA **ligands** may be prepd. after the identification of 2'-OH RNA **ligands** or by performing **SELEX** using a candidate mixt. of modified RNAs. For example, 2'-NH2 pyrimidine RNA **ligands** to VEGF are described. The present invention includes the method of identifying **nucleic** acid **ligands** and **ligand** sequences to VEGF.

L79 ANSWER 15 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:783978 HCAPLUS
DN 130:149457
TI A comprehensive **library** of DNA-binding site matrixes for 55 proteins applied to the complete Escherichia coli K-12 genome
AU Robison, Keith; McGuire, Abigail Manson; Church, George M.
CS Department of Genetics, Harvard Medical School, Boston, MA, 02115, USA
SO J. Mol. Biol. (**1998**), 284(2), 241-254
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press
DT Journal
LA English
AB A major mode of gene regulation occurs via the binding of specific proteins to specific DNA sequences. The availability of complete bacterial genome sequences offers an unprecedented opportunity to describe networks of such interactions by correlating existing exptl. data with computational predictions. Of the 240 candidate Escherichia coli DNA-binding proteins, about 55 have DNA-binding sites identified by DNA footprinting. We used these sites to construct recognition matrixes, which we used to search for addnl. binding sites in the E. coli genomic sequence. Many of these matrixes show a strong preference for non-coding

DNA. Discrepancies are identified between matrixes derived from natural sites and those derived from **SELEX** (**Systematic Evolution** of **Ligands** by **Exponential enrichment**) expts. We have constructed a database of these proteins and binding sites, called DPInteract (available at http://arep.med.harvard.edu/dpinteract). (c) 1998 Academic Press.

L79 ANSWER 16 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:692184 HCAPLUS
DN 130:76652
TI Generation and selection of RNA **ligands** that inhibit the interaction of vascular permeability factor/vascular endothelial growth factor (VPF/VEGF) with its receptors
AU Green, Louis S.; Janjic, Nebojsa
CS Nexstar Pharmaceuticals, Boulder, CO, 80301, USA
SO Growth Factors Recept. (**1998**), 125-148. Editor(s): McKay, Ian A.; Brown, Kenneth D. Publisher: Oxford University Press, Oxford, UK. CODEN: 66VTA8
DT Conference; General Review
LA English
AB A review with 49 refs. The **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) process has recently emerged as a powerful method for screening sequence-randomized nucleic acid **libraries** for rare mols. (aptamers) that bind with high affinity and specificity to a variety of target mols., by successive rounds of affinity selection and amplification. VPF/VEGF was chosen as a **SELEX** target because it is a potent inducer of angiogenesis (the growth of new blood vessels) in vivo. As we enter a phase in which VPF/VEGF and other aptamers are being tested in a no. of animal efficacy models, the dream of having a robust technol. that rapidly produces drug candidates is coming closer to reality.

L79 ANSWER 17 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:545366 HCAPLUS
DN 129:145623
TI **Systematic evolution** of **ligands** by **exponential enrichment**: tissue **SELEX**
IN Jensen, Kirk B.; Chen, Hang; Morris, Kevin N.; Stephens, Andrew; Gold, Larry
PA NeXstar Pharmaceuticals, Inc., USA
SO U.S., 63 pp. Cont.-in-part of U. S. 5,475,096. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5789157	A	19980804	US 1995-434425	19950503 <--
	US 5475096	A	19951212	US 1991-714131	19910610 <--
	EP 786469	A2	19970730	EP 1997-200035	19910610 <--
	EP 786469	A3	19970806		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	IL 112141	A1	19980405	IL 1991-112141	19910611 <--
	US 5496938	A	19960305	US 1992-964624	19921021 <--
	CA 2219807	AA	19961107	CA 1996-2219807	19960501 <--
	WO 9634875	A1	19961107	WO 1996-US6060	19960501 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
	AU 9656707	A1	19961121	AU 1996-56707	19960501 <--
	EP 823914	A1	19980218	EP 1996-913880	19960501 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
US 6013443 A 20000111 US 1997-906955 19970805 <--
PRAI US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-964624 19921021 <--
EP 1991-912753 19910610 <--
IL 1991-98456 19910611 <--
US 1995-433585 19950503 <--
US 1995-434001 19950503 <--
US 1995-434425 19950503 <--
US 1995-437667 19950503 <--
WO 1996-US6060 19960501 <--
AB This invention discloses high-affinity oligonucleotide **ligands** to complex tissue targets, specifically nucleic acid **ligands** having the ability to bind to complex tissue targets, and the methods for obtaining such **ligands**. Tissue targets comprise cells, subcellular components, aggregates or cells, collections of cells, and higher ordered structures. Specifically, nucleic acid **ligands** to red blood cell ghosts, glioblastomas, and lymphomas are described.

L79 ANSWER 18 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:542718 HCAPLUS
DN 129:171485
TI Method for obtaining RNA aptamers by shape selection rather than by base pairing
IN Schmidt, Francis J.; Cho, Bongrae; Nicholas, Jr Hugh B.
PA The Curators of the University of Missouri, USA
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5792613	A	19980811	US 1996-662335	19960612 <--

AB A method of using **SELEX** to select for RNA aptamers that bind to a specific shape rather than to a specific sequence is described. Selection of RNA aptamers with extensive Watson-Crick complementarity to the nucleic acid **ligand** is precluded by inclusion of a blocking oligodeoxynucleotide in the binding phase of the selection protocol.

L79 ANSWER 19 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:405419 HCAPLUS
DN 129:78838
TI **Systematic evolution** of **ligands** by **exponential enrichment**: photoselection of nucleic acid **ligands** and solution **SELEX**
IN Gold, Larry; Willis, Michael; Koch, Tad; Ringquist, Steven; Jensen, Kirk; Atkinson, Brent
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 69 pp. Cont.-in-part of U.S. Ser. No. 143,564, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763177	A	19980609	US 1996-612895	19960308 <--
US 5475096	A	19951212	US 1991-714131	19910610 <--
EP 786469	A2	19970730	EP 1997-200035	19910610 <--
EP 786469	A3	19970806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 112141	A1	19980405	IL 1991-112141	19910611 <--
US 5270163	A	19931214	US 1992-931473	19920817 <--
WO 9508003	A1	19950323	WO 1994-US10562	19940916 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU,				

JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, US, UZ, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRAI US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-931473 19920817 <--
US 1993-123935 19930917 <--
US 1993-143564 19931025 <--
WO 1994-US10562 19940916 <--
EP 1991-912753 19910610 <--
IL 1991-98456 19910611 <--

AB A method for identifying nucleic acid **ligands** to target mols. using the **SELEX** (**Systematic Evolution** of **Ligands** by **Exponential enrichment**) procedure wherein the candidate nucleic acids contain photoreactive groups and nucleic acid **ligands** identified thereby are claimed. The complexes of increased affinity nucleic acids and target mols. formed in the procedure are crosslinked by irradn. to facilitate sepn. from unbound nucleic acids. In other methods partitioning of high and low affinity nucleic acids is facilitated by primer extension steps as shown in the figure in which chain termination nucleotides, digestion resistant nucleotides or nucleotides that allow retention of the cDNA product on an affinity matrix are differentially incorporated into the cDNA products of either the high or low affinity nucleic acids and the cDNA products are treated accordingly to amplification, enzymic or chem. digestion or by contact with an affinity matrix.

L79 ANSWER 20 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:392081 HCAPLUS
DN 129:25080
TI Nucleic acid **ligands** as high-affinity inhibitors of HIV integrase
IN Allen, Patrick; Gold, Larry
PA NeXstar Pharmaceuticals, Inc., USA
SO U.S., 25 pp. Cont.-in-part of U. S. 5,475,096.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5756287	A	19980526	US 1994-361795	19941221 <--
US 5475096	A	19951212	US 1991-714131	19910610 <--
EP 786469	A2	19970730	EP 1997-200035	19910610 <--
EP 786469	A3	19970806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 112141	A1	19980405	IL 1991-112141	19910611 <--
US 5496938	A	19960305	US 1992-964624	19921021 <--
WO 9530775	A1	19951116	WO 1995-US5600	19950503 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9524702	A1	19951129	AU 1995-24702	19950503 <--
US 5587468	A	19961224	US 1995-442572	19950516 <--
US 5635615	A	19970603	US 1995-477530	19950607 <--
US 5654151	A	19970805	US 1995-477830	19950607 <--

PRAI US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-964624 19921021 <--
US 1993-117991 19930908 <--
EP 1991-912753 19910610 <--

IL 1991-98456 19910611 <--
US 1992-931473 19920817 <--
US 1994-238863 19940506 <--
US 1994-248632 19940524 <--
US 1994-303362 19940909 <--
US 1994-361795 19941221 <--
WO 1995-US5600 19950503 <--
US 1995-447172 19950519 <--

AB Methods are described for the identification and prepn. of nucleic acid **ligands** to HIV integrase. Included in the invention are 55 specific RNA **ligands** to HIV integrase identified by the **SELEX** method (**systematic evolution** of **ligands** by **exponential enrichment**). Also included in the invention are specific RNA **ligands** that are inhibitors of HIV integrase.

L79 ANSWER 21 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:349417 HCAPLUS
DN 129:89841
TI The mathematics of **SELEX** against complex targets
AU Vant-Hull, Barry; Payano-Baez, Antonio; Davis, Robert H.; Gold, Larry
CS Department of Molecular Cellular, and Developmental Biology, University of Colorado, Boulder, CO, 80309, USA
SO J. Mol. Biol. (**1998**), 278(3), 579-597
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press Ltd.
DT Journal
LA English
AB The authors have developed a computer model for the simulation of simultaneous **SELEX** (**Systemic Evolution** of **Ligands** by **Exponential enrichment**) against multiple targets. The model assumes equil. behavior for the formation of binary **ligand**:target complexes, and that there is no **ligand**:**ligand** or target:target interaction. Target concns., **ligand** concns., and affinity distributions of the initial **ligand** pool for each individual target may be set by the user. The authors have used this program to gain an understanding of how the presence of multiple targets affects the selection process. In most cases, the authors find the **SELEX** is capable of generating different **ligands** for the different targents in a heterogeneous mixt., regardless of large variations in target concns. and **ligand** :target affinities. A low relative partitioning efficiency (the efficiency with which **ligands** complexed with a target are sepd. from free **ligands**) for a target in a mixt. gives a greatly reduced rate of selection of high-affinity **ligands** to that target. The ratio of each high-affinity **ligand** to its individual target within a pool of **ligands** selected for binding against a mixt. of targets is approx. proportional to the concn. of the target multiplied by the **ligand**:target partitioning efficiency. The use of the method for high-throughput drug screening of combinatorial **libraries** is discussed.

L79 ANSWER 22 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:289288 HCAPLUS
DN 129:63647
TI Stochastic modeling and optimization of phage display
AU Levitan, Bennett
CS Santa Fe Institute, Santa Fe, NM, 87501, USA
SO J. Mol. Biol. (**1998**), 277(4), 893-916
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press Ltd.
DT Journal
LA English
AB Phage display, **SELEX** and other methods of combinatorial chem. have become very popular means of finding **ligands** with high affinities to given targets. Despite their success, they suffer from

numerous sources of error and bias, such as very low initial concns. of species, nonspecific binding, and the sampling of only a tiny fraction of the **library** at the end of an expt. To understand the interaction of these errors and to better devise mol. search strategies that take the errors into account, I devise and analyze a highly detailed model of phage display. The model is specifically designed to study the influence of the stochastic nature of each lab. step. The model includes phage multivalency, multiple classes of targets, and solid-phase equil. and washing, yet it is amenable to analytic results and rapid computer simulation. With both analytic and simulation approaches, I: (1) describe the effects of target concn., phage valency, degree of background binding and other lab. parameters on the probabilities of phage binding and of being selected; (2) show the effects of an increasing selection stringency strategy and how it results in a tradeoff between rapid **library** enrichment and high probability of sampling the best **ligands**; and (3) show how the no. of phage sampled for detailed study at the end of a search alters search success. The work concludes with several practical suggestions for the control of selection stringency.

L79 ANSWER 23 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:162219 HCAPLUS
DN 128:238872
TI Progress towards therapeutic application of **SELEX**-derived aptamers
AU Polisky, Barry
CS NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SO Many Faces RNA, [SmithKline Beecham Pharm. Res. Symp.], 8th (**1998**), 161-177. Editor(s): Eggleston, Drake S.; Prescott, Catherine D.; Pearson, Neil D. Publisher: Academic Press, San Diego, Calif. CODEN: 65SLAU
DT Conference; General Review
LA English
AB A review with 56 refs. **SELEX** is a combinatorial **ligand** discovery technol. that utilizes large **libraries** of random sequence oligonucleotides to isolate **ligands** with high affinity and specificity to mol. targets. These **ligands** are known as aptamers. **SELEX** has been used to isolate aptamers to a broad range of targets ranging from small org. mols. such as theophylline to proteins involved in pathol. processes. **Libraries** are commonly composed of either DNA or modified RNA. An RNA modification conferring extensive in vivo stability relative to unmodified RNA is substitution of the 2'-OH with 2'-F on pyrimidine nucleotides. Such **libraries** are chem. stable upon prolonged incubation with a variety of biol. sources including human plasma. Affinities of selected aptamers for growth factors and certain cell adhesion mols. are typically in the low nM to pM Kd range. Nuclease-stable aptamer antagonists to human growth factors responsible for neo-angiogenesis such as VEGF, bFGF and PDGF, and to cell adhesion mols. such as L- and P-selectin, have been isolated and tested in a variety of in vitro and in vivo model systems. Aptamers to the growth factors block their interaction with cognate receptors on cell surfaces in cell culture. Aptamers to selectins have been shown to recognize the carbohydrate domains and bind to selectins on cell surfaces. Methodol. to identify specific contact positions between aptamers and targets has been developed utilizing both photochem. and soln. chem. Examples of both types are presented. Interactions of specific aptamers with cognate targets are described as well as progress in defining higher order structural motifs of aptamer-target complexes.

L79 ANSWER 24 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:119594 HCAPLUS
DN 128:238959
TI High-Affinity Aptamers Selectively Inhibit Human Nonpancreatic Secretory Phospholipase A2 (hnps-PLA2)
AU Bridonneau, Philippe; Chang, Ying-Fon; O'Connell, Dan; Gill, Stanley C.; Snyder, David W.; Johnson, Lea; Goodson, Theodore, Jr.; Herron, David K.; Parma, David H.

CS NeXstar Pharmaceuticals Inc., Boulder, CO, 80301, USA
SO J. Med. Chem. (**1998**), 41(6), 778-786
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A family of sequence-related 2'-aminopyrimidine, 2'-hydroxylpurine aptamers, developed by oligonucleotide-based combinatorial chem., **SELEX** (**systematic evolution** of **ligand** by **exponential enrichment**) technol., binds human nonpancreatic secretory phospholipase A2 (hnps-PLA2) with nanomolar affinities and inhibits enzymic activity. Aptamer 15, derived from the family, binds hnps-PLA2 with a Kd equal to 1.7 .+-. 0.2 nM and, in a std. chromogenic assay of enzymic activity, inhibits hnps-PLA2 with an IC50 of 4 nM, at a mole fraction of substrate concn. of 4 .times. 10-6 and a calcd. Ki of 0.14 nM. Aptamer 15 is selective for hnps-PLA2, having a 25- and 2500-fold lower affinity, resp., for the unrelated proteins human neutrophil elastase and human IgG. Contractions of guinea pig lung pleural strips induced by hnps-PLA2 are abolished by 0.3 .mu.M aptamer 15, whereas contractions induced by arachidonic acid are not altered. The structure that is essential for binding and inhibition appears to be a 40-base hairpin/loop motif with an asym. internal loop. The affinity and activity of the aptamers demonstrate the ability of the **SELEX** process to isolate antagonists of nonnucleic-acid-binding proteins from vast oligonucleotide combinatorial **libraries**.

L79 ANSWER 25 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:115365 HCAPLUS
DN 128:150369
TI **Systematic evolution** of **ligands** by **exponential enrichment**: tissue **SELEX**
IN Jensen, Kirk B.; Chen, Hang; Morris, Kevin N.; Stephens, Andrew; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO U.S., 63 pp. Cont.-in-part of U.S. 5,475,096.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5712375	A	19980127	US 1995-434001	19950503	<--
	US 5475096	A	19951212	US 1991-714131	19910610	<--
	EP 786469	A2	19970730	EP 1997-200035	19910610	<--
	EP 786469	A3	19970806			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	IL 112141	A1	19980405	IL 1991-112141	19910611	<--
	US 5496938	A	19960305	US 1992-964624	19921021	<--
	CA 2219807	AA	19961107	CA 1996-2219807	19960501	<--
	WO 9634875	A1	19961107	WO 1996-US6060	19960501	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI					
	AU 9656707	A1	19961121	AU 1996-56707	19960501	<--
	EP 823914	A1	19980218	EP 1996-913880	19960501	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 11505106	T2	19990518	JP 1996-532024	19960501	<--
PRAI	US 1990-536428	19900611	<--			
	US 1991-714131	19910610	<--			
	US 1992-964624	19921021	<--			
	EP 1991-912753	19910610	<--			
	IL 1991-98456	19910611	<--			

US 1995-433585 19950503 <--
US 1995-434001 19950503 <--
US 1995-434425 19950503 <--
US 1995-434667 19950503 <--
US 1995-437425 19950503 <--
US 1995-437667 19950503 <--
WO 1996-US6060 19960501 <--

AB This invention discloses high-affinity oligonucleotide **ligands** to complex tissue targets, specifically nucleic acid **ligands** having the ability to bind to complex tissue targets, and the methods for obtaining such **ligands**. Tissue targets comprise cells, subcellular components, aggregates or cells, collections of cells, and higher ordered structures. Specifically, nucleic acid **ligands** to red blood cell ghosts, glioblastomas, and lymphomas are described.

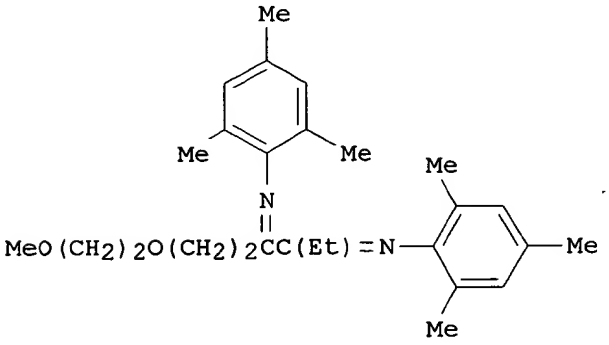
L79 ANSWER 26 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:108554 HCAPLUS
DN 128:291926
TI Activation of 2'-5' oligoadenylate synthetase by single-stranded and double-stranded RNA aptamers
AU Hartmann, Rune; Norby, Peder L.; Martensen, Pia M.; Jorgensen, Poul; James, Marion C.; Jacobsen, Christian; Moestrup, Soren K.; Clemens, Michael J.; Justesen, Just
CS Department Molecular Structural Biology, University Aarhus, Aarhus C, DK-8000, Den.
SO J. Biol. Chem. (**1998**), 273(6), 3236-3246
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB A no. of small RNA mols. that are high affinity **ligands** for the 46-kDa form of human 2'-5' oligoadenylate synthetase have been identified by the **SELEX** method. Surface plasmon resonance anal. indicates that these RNAs bind to the enzyme with dissocn. consts. in the nanomolar range. Competition expts. indicate that the binding site for the small RNAs on the 2'-5' oligoadenylate synthetase mol. at least partially overlaps that for the synthetic double-stranded RNA, poly(I).cntdot.poly(C). Several of the RNAs function as potent activators of 2'-5' oligoadenylate synthetase in vitro, although there is no correlation between binding affinity and ability to activate. The RNA aptamers having the strongest activation potential appear to have few base-paired regions. This suggest that 2'-5' oligoadenylate synthetase, which has previously been believed to be activated only by double-stranded RNA, can also be activated by RNA **ligands** with little secondary structure. Since 2'-5' oligoadenylate synthetase possesses no homol. to other known RNA-binding proteins, the development of small specific **ligands** by **SELEX** should facilitate studies of RNA-protein interactions and may reveal novel features of the structure-function relationships involving this enzyme.

L79 ANSWER 27 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:87740 HCAPLUS
DN 128:141181
TI Combinatorial synthesis and analysis of **organometallic** compounds and olefin polymerization catalysts
IN Weinberg, W. Henry; McFarland, Eric; Goldwasser, Isy; Boussie, Thomas; Turner, Howard; Van Beek, Johannes A. M.; Murphy, Vince; Powers, Timothy; et al.
PA Symyx Technologies, USA; Weinberg, W. Henry; McFarland, Eric; Goldwasser, Isy; Boussie, Thomas; Turner, Howard; Van Beek, Johannes A. M.; Murphy, Vince; Powers, Timothy
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9803521	A1	19980129	WO 1997-US13312	19970722 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9737418	A1	19980210	AU 1997-37418	19970722 <--
	EP 923590	A1	19990623	EP 1997-934335	19970722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE, FI				
	JP 11514012	T2	19991130	JP 1997-507246	19970722 <--
	EP 978499	A2	20000209	EP 1999-203632	19970722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 983983	A2	20000308	EP 1999-203631	19970722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 985678	A2	20000315	EP 1999-203630	19970722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI	US 1996-16102	19960723 <--
	US 1996-28106	19961009 <--
	US 1996-29255	19961025 <--
	US 1997-35366	19970110 <--
	US 1997-48987	19970609 <--
	EP 1997-934335	19970722 <--
	WO 1997-US13312	19970722 <--

GI



I

AB **Libraries** of unsupported and supported metal-**ligand** compds., useful for homogeneous and heterogeneous olefin polymn. catalysts, resp., are manufd. by combinatorial synthesis. Thus, complexation of diimine I with (DME)NiBr2 in 24 h in CH2Cl2 gave a product, and polymn. of ethylene gas 2.25 h in PhMe in the presence of MAO gave 1.38 g polymer.

L79 ANSWER 28 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:65818 HCAPLUS
DN 128:136534
TI Oligonucleotides as inhibitors of selectins, selection thereof, and therapeutic use
IN Koenig, Andrea; Varki, Ajit; Parma, David; Hicke, Brian J.
PA Regents of the University of California, USA; Koenig, Andrea; Varki, Ajit; Parma, David; Hicke, Brian J.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9801140	A1	19980115	WO 1997-US10267	19970611 <--
	W: CA, JP, US, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 1996-19552	19960611 <--			
	US 1996-33149	19961213 <--			

AB Disclosed are oligonucleotides and methods for inhibiting selectins. The oligonucleotides (aptamers) of the invention specifically bind L-selectin and can be isolated by **systematic evolution** of **ligands** by **exponential enrichment** (**SELEX**) technol. Preferably, the method involves noncovalently binding the selectin receptor globulin to protein A sepharose beads. The oligonucleotides are useful for blocking selectin-dependent interactions with natural **ligands** in vivo and for diagnostic tests in vitro-cell surface and sol. selections. Clin., the oligonucleotides can be administered to patients in methods for treating a variety of inflammatory and post-ischemic pathologies, such as ischemia-reperfusion injury, acute inflammatory states, and chronic immune responses. A specific modification of the previously described modifications are: (a) carrying out binding at anion concns. < 160 mM, i.e., close to physiol.; (b) eluting by chelating Ca++, thereby obtaining oligonucleotides binding the Ca++-dependent lectin domain; (c) using low 1-5 mM EDTA for elution, avoiding nonspecific elution; (d) doing selection at 22-37 .degree.C to avoid loss of **ligand** structure if initial selection is done at 4 .degree.C.

L79 ANSWER 29 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:735877 HCAPLUS
DN 128:10869
TI Identification of oligonucleotide **ligands** for biomolecules for diagnostic, therapeutic, or research use from completely random **libraries**
IN Bruice, Thomas W.; Lima, Walter F.
PA ISIS Pharmaceuticals, Inc., USA
SO U.S., 22 pp. Cont.-in-part of U.S. Ser. No. 755,485, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5686242	A	19971111	US 1994-330000	19941027 <--
	US 6022691	A	20000208	US 1997-965908	19971107 <--
PRAI	US 1991-755485	19910905 <--			
	WO 1992-US7489	19920904 <--			
	US 1994-330000	19941027 <--			

AB Oligonucleotides that selectively bind to target biomols. are detd. by in vitro assay of a pool of random oligonucleotides for their binding to the target biomol. followed by recovery and characterization of selected oligonucleotides. The oligonucleotides have as large a random sequence as possible and may be completely random or may have a 5'-poly(A) tail that can be used for oligo(dT)-directed formation of a cDNA followed by PCR amplification of the products. The binding and sequence of the oligonucleotide may then be characterized by affinity cleavage. These oligonucleotides may be used for therapeutic, diagnostic and research reagent purposes.

L79 ANSWER 30 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:706957 HCAPLUS
DN 128:31741
TI Oligonucleotide inhibitors of human thrombin that bind distinct epitopes
AU Tasset, Diane M.; Kubik, Mark F.; Steiner, Walter

CS NeXstar Pharmaceuticals, Inc, Boulder, CO, 80301, USA
SO J. Mol. Biol. (**1997**), 272(5), 688-698
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic
DT Journal
LA English
AB Thrombin, a multifunctional serine protease, recognizes multiple macro-mol. substrates and plays a key role in both procoagulant and anticoagulant functions. The substrate specificity of thrombin involves two electropos. surfaces, the fibrinogen-recognition and heparin-binding exosites. The **SELEX** process is a powerful combinatorial methodol. for identifying high-affinity oligonucleotide **ligands** to any desired target. The **SELEX** process has been used to isolate single-stranded DNA **ligands** to human thrombin. Here, a 29-nucleotide single-stranded DNA **ligand** to human thrombin, designated 60-18[29], with a Kd of approx. 0.5 nM is described. DNA 60-18[29] inhibits thrombin-catalyzed fibrin clot formation in vitro. Previously described DNA **ligands** bind the fibrinogen-recognition exosite, while competition and photocrosslinking expts. indicate that the DNA **ligand** 60-18[29] binds the heparin-binding exosite. DNA 60-18[29] is a quadruplex/duplex with a 15-nucleotide "core" sequence that has striking similarity to previously described DNA **ligands** to thrombin, but binds with 20 to 50-fold higher affinity. The 15-nucleotide core sequence has eight highly conserved guanine residues and forms a G-quadruplex structure. A single nucleotide within the G-quadruplex structure can direct the DNA to a distinct epitope. Addnl. sequence information in the duplex regions of **ligand** 60-18[29] contribute to greater stability and affinity of binding to thrombin. A low-resoln. model for the interaction of DNA 60-18[29] to human thrombin has been proposed.

L79 ANSWER 31 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:511999 HCAPLUS
DN 127:117370
TI Screening **natural** samples for new therapeutic and diagnostic compounds using capillary electrophoresis
IN Hughes, Dallas E.; Karger, Barry L.
PA Northeastern University, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9722000	A1	19970619	WO 1996-US19779	19961210	<--
	W: CA, JP					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5783397	A	19980721	US 1996-662085	19960612	<--
	CA 2239418	AA	19970619	CA 1996-2239418	19961210	<--
	EP 876609	A1	19981111	EP 1996-944795	19961210	<--
	R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE					
	JP 2000502443	T2	20000229	JP 1997-522198	19961210	<--
PRAI	US 1995-8503	19951211	<--			
	US 1996-662085	19960612	<--			
	WO 1996-US19779	19961210	<--			

AB A method in which natural sample components are simultaneously fractionated and screened for compds. that bind tightly to specific mols. of interest is disclosed. Such newly isolated **ligands** are good candidates for potential therapeutic or diagnostic compds. The natural sample is first combined with a potential target mol. and then subjected to capillary electrophoresis (CE). Charged (or even neutral) compds. present in the natural sample that bind to the added target mol. can alter its normal migration time upon CE, by changing its charge-to-mass ratio, or will cause a variation in peak shape or area. Complex formation can be detected by simply monitoring the migration of the target mol. during

electrophoresis. Any new **ligands** that bind to the target mol. will be good candidates for therapeutic or diagnostic compds. Interfering, weak-binding **ligands** commonly present in crude exts. are not detected. Small, neutral **ligands**, as well as charged **ligands**, can be identified in competitive binding expts. with known, charged competitor mols.

L79 ANSWER 32 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:444913 HCAPLUS
DN 127:186215
TI Interacting RNA species identified by combinatorial selection
AU Cho, Bongrae; Taylor, David C.; Nicholas, Hugh B., Jr; Schmidt, Francis J.
CS Department of Biochemistry, University of Missouri-Columbia, Columbia, MO, 65212, USA
SO Bioorg. Med. Chem. (**1997**), 5(6), 1107-1113
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
AB RNA mols. were selected from a random sequence **library** for their ability to bind to an RNA stem-loop target. Oligonucleotides with extensive Watson-Crick complementarity to the RNA **ligand** were selected against by inclusion of a blocking oligodeoxynucleotide in the binding phase of the selection protocol. After 18 generations of **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) a single RNA family was predominant in the binding population. The winning aptamer RNA bound the target RNA with an apparent Kd = 70 nM. Structural mapping and Fe(II)-EDTA protection indicated that the target RNA interacted with small unpaired loops in the aptamer structure.

L79 ANSWER 33 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:444911 HCAPLUS
DN 127:149345
TI Post-**SELEX** combinatorial optimization of aptamers
AU Eaton, Bruce E.; Gold, Larry; Hicke, Brian J.; Janjic, Nebojsa; Jucker, Fiona M.; Sebesta, David P.; Tarasow, Theodore M.; Willis, Michael C.; Zichi, Dominic A.
CS NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SO Bioorg. Med. Chem. (**1997**), 5(6), 1087-1096
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
AB In vitro selection techniques provide a means of isolating nucleic acid **ligands** for binding to particular protein targets. Although most aptamers have quite high affinities for their target proteins, it has been shown that post-**SELEX** modification can result in further enhancement of binding affinity, as well as other desired properties. This has led to the current development of a more systematic approach to aptamer optimization using a combinatorial screening methodol.

L79 ANSWER 34 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:421636 HCAPLUS
DN 127:76973
TI Production of chimeric multi-functional nucleic acids using nucleic acid **library** selection through **SELEX** procedure followed by linking nucleic acids of different **libraries**
IN Burke, Donald; Tarasow, Ted; Eaton, Bruce E.; Gold, Larry
PA NeXstar Pharmaceuticals, Inc., USA
SO U.S., 15 pp. Cont.-in-part of U.S. 5,475,096.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 81
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	US 5637459	A	19970610	US 1994-284063	19940802 <--
	US 5475096	A	19951212	US 1991-714131	19910610 <--
	EP 786469	A2	19970730	EP 1997-200035	19910610 <--
	EP 786469	A3	19970806		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	IL 112141	A1	19980405	IL 1991-112141	19910611 <--
	US 5773598	A	19980630	US 1995-464102	19950605 <--
	WO 9604403	A1	19960215	WO 1995-US9446	19950726 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9531495	A1	19960304	AU 1995-31495	19950726 <--
PRAI	US 1990-536428	19900611 <--			
	US 1991-714131	19910610 <--			
	EP 1991-912753	19910610 <--			
	IL 1991-98456	19910611 <--			
	US 1994-284063	19940802 <--			
	WO 1995-US9446	19950726 <--			

AB Methods are disclosed for producing chimeric nucleic acid mols. with two or more functions. One embodiment of the invention is described here. A first **library** of nucleic acids selected through the **SELEX** procedure for a first function is generated and the nucleic acids have a 3' fixed sequence. A second **library** of nucleic acids selected through the **SELEX** procedure for a second function is generated and the nucleic acids have a 5' fixed sequence identical to the 3' fixed sequence of the nucleic acids of the first **library**. The first and second **libraries** are mixed under conditions which promote interlibrary annealing, forming chimeric nucleic acid mols. by enzymically extending the recessed 3' ends while copying the 5' extensions of each annealed pair. Chimeric nucleic acids are then amplified to generate double-stranded DNA. Chem. schemes for linking different oligonucleotides of different **libraries** are also included. An example describes the 3'-3'-linking of nucleic acids using GMP and benzaldehyde di-Me acetal. The chimeric mols. of this invention are useful in a variety of ways, including having improved affinities for a target mol., enhancing assembly of multi-component mols., and promoting reactions between two mols.

L79 ANSWER 35 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:414427 HCAPLUS
DN 127:185519
TI Isolation and characterization of 2'-fluoro-, 2'-amino-, and 2'-fluoro-/amino-modified RNA **ligands** to human IFN-.gamma. that inhibit receptor binding
AU Kubik, Mark F.; Bell, Carol; Fitzwater, Tim; Watson, Susan R.; Tasset, Diane M.
CS NeXstar Pharmaceuticals, Boulder, CO, 80301, USA
SO J. Immunol. (**1997**), 159(1), 259-267
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB CD4+ Th cells produce cytokines that play a pivotal role in the induction and regulation of cell-mediated and humoral immunity. Th1 cells, characterized by their secretion of IFN-.gamma., induce macrophage cytotoxicity, delayed hypersensitivity, and enhanced cellular immunity. Secretion of IFN-.gamma. may even suppress Th2-enhanced humoral immunity. A counterproductive Th1 response and concomitant secretion of IFN-.gamma. may result in inflammatory and autoimmune diseases. IFN-.gamma. regulation of T cell function has potential for therapeutic intervention. To isolate high affinity oligonucleotide inhibitors of IFN-.gamma.

activity, combinatorial **libraries** of RNA mols. modified at the 2' position of pyrimidine nucleotides with fluoro (F), amino (NH2), or a mixt. of F and NH2 (2'-F/NH2) were screened using the **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) combinatorial chem. process. Each modified **library** of RNA mols. provides an expanded repertoire of mols. with increased structural diversity and unique binding properties. This added diversity increases the possibility of isolating mols. with the desired functional properties. These RNAs modified at the 2' position have also been shown to nuclease resistant. High affinity **ligands** to human IFN-.gamma. from each modified **library** were isolated and characterized. The Kds of these **ligands** were detd. and their secondary structures were predicted. The specificity of these **ligands** for IFN-.gamma. binding was confirmed, and their ability to inhibit binding of IFN-.gamma. to its receptor on A549 human lung carcinoma cells was detd. A 2'-NH2-modified **ligand** (2'-NH2-30) is described that binds IFN-.gamma. with high affinity and inhibits IFN-.gamma.-induced expression of MHC class I and ICAM-1 by human myeloid leukemia cells.

L79 ANSWER 36 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:341254 HCAPLUS
DN 127:29674
TI Recognition of **DNA** sequence and **DNA** bending. Molecular design for artificial repressor
AU Sugiura, Yukio; Nagaoka, Makoto
CS Inst. Chem. Res., Kyoto Univ., Uji, 611, Japan
SO Yuki Gosei Kagaku Kyokaishi (**1997**), 55(5), 384-392
CODEN: YGKKAE; ISSN: 0037-9980
PB Yuki Gosei Kagaku Kyokai
DT Journal; General Review
LA Japanese
AB A review with 32 refs. **DNA** recognition is a very important phenomenon in biol. and chem., and the mol. basis of the sequence-specific **DNA** binding is the subject of investigations aimed at the rational design of mols. with specific biol. activities. Minor-**groove** -binding **polyamides** contg. N-methylimidazole and N-methylpyrrole amino acids achieve affinities and specificities comparable to **DNA** binding proteins. The synthetic oligosaccharide moiety of the antibiotic calicheamicin and the head-to-head dimer of this oligosaccharide bind to the minor **groove** of **DNA** in a sequence-selective manner preferring distinct target sequences. Zinc-finger **libraries** with different **DNA**-binding specificities based on a one-finger-three-nucleotide code have been developed successfully. On the other hand, **DNA** bending is also important regulators of biol. process. Sequence-specific **DNA** bending **ligands** are designed to bind 2 noncontiguous sites in the major **groove** and induce a bent in the **DNA**. Mols. that specifically bind and bent any predetd. **DNA** sequence in the human genome would be useful tools in mol. biol. and potentially in human medicine.

L79 ANSWER 37 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:159485 HCAPLUS
TI Determination of DNA binding specificity of regulatory proteins.
AU Maillet, Andrew L.; Hamilton, Douglas A.; Nagel, Walter O.
CS Department Chemistry, Hartwick College, Oneonta, NY, 13820, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (**1997**), CHED-194 Publisher: American Chemical Society, Washington, D. C.
CODEN: 64AOAA
DT Conference; Meeting Abstract
LA English
AB The process called **SELEX**, an acronym for Selective Evolution of **Ligand** by EXponential enrichment, is a combinatorial approach to the study of protein-nucleic acid interactions and the rational design of **ligands** to proteins or other target mols. The process involves

obtaining a randomized oligonucleotide **library**, and subsequently placing the random pool under selective pressure, reproducing only those oligonucleotides which are successful. We have tested the procedure using EcoRI methylase, a well studied DNA binding protein. The methylase binds double-stranded DNA at the palindromic hexamer, GAATTC. We will present the results of the **SELEX** procedure directed at the EcoRI methylase and also at a regulatory protein of basic research interest. The application, efficiency and utility of the procedure will be discussed

L79 ANSWER 38 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:101635 HCAPLUS
DN 126:101475
TI Method and apparatus for determining consensus secondary structures for nucleic acid sequences
IN Davis, Jeffrey P.; Janjic, Nebojsa; Zichi, Dominic A.
PA Nexstar Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9639539	A1	19961212	WO 1996-US9452	19960606 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	US 5843732	A	19981201	US 1995-470939	19950606 <--
	AU 9661599	A1	19961224	AU 1996-61599	19960606 <--
PRAI	US 1995-470939		19950606 <--		
	WO 1996-US9452		19960606 <--		

AB A dot matrix display is utilized to visualize consensus structures of functionally related sequence sets. The functionally related sequence sets are screened from an oligonucleotide **library** to identify a plurality of oligonucleotides having a select functional property. The identified plurality of oligonucleotides are then analyzed to identify a nucleotide sequence for each oligonucleotide. The oligonucleotides are than aligned according to primary structural similarity. A matrix representing the relative strength of a select property between nucleotides of each aligned oligonucleotide sequence is then constructed. The matrix representing the relative strength of the select property is analyzed to identify high-strength consensus structures, and this information is translated to a consensus secondary structure. The matrix is preferably constructed through the use of a digital computer. The visual display of the matrix representing relative strength of the select property is preferably accomplished by means of a color monitor (relative strength being indicated by select colors). Interactive features are provided for editing the overall sequence alignment, display editing that allows progressive filtering or pruning of the display from complex (all inclusive) to simpler (showing only the most conserved and most stable regions), easy identification of mutually exclusive structures, detection of base pairing covariation, and detection of G-quartet structures. The **system** is demonstrated by **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) RNA sequences that were selected for high-affinity binding to basic fibroblast growth factor, RNA mols. selected for high affinity binding to the bronchodilator theophylline, sequence-related RNA mols. that bind to HIV-1 reverse transcriptase with high affinity, a set of sequences contg. modified ribose moieties for pyrimidine bases (2'-amino-RNA), and by application to mol. taxonomy of a set of 40 tRNA mols.

L79 ANSWER 39 OF 60 HCAPLUS COPYRIGHT 2000 ACS

AN 1997:55968 HCAPLUS
DN 126:70128
TI **Systematic evolution** of **ligands** by **exponential enrichment**: tissue **SELEX**
IN Jensen, Kirk B.; Chen, Hang; Morris, Kevin N.; Stephens, Andrew; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA; Jensen, Kirk B.; Chen, Hang; Morris, Kevin N.; Stephens, Andrew; Gold, Larry
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9634875	A1	19961107	WO 1996-US6060	19960501 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
	US 5712375	A	19980127	US 1995-434001	19950503 <--
	US 5763566	A	19980609	US 1995-433585	19950503 <--
	US 5789157	A	19980804	US 1995-434425	19950503 <--
	US 5864026	A	19990126	US 1995-437667	19950503 <--
	AU 9656707	A1	19961121	AU 1996-56707	19960501 <--
	EP 823914	A1	19980218	EP 1996-913880	19960501 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11505106	T2	19990518	JP 1996-532024	19960501 <--
	US 6013443	A	20000111	US 1997-906955	19970805 <--

PRAI US 1995-433585 19950503 <--
US 1995-434001 19950503 <--
US 1995-434425 19950503 <--
US 1995-437667 19950503 <--
US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-964624 19921021 <--
US 1995-434667 19950503 <--
US 1995-437425 19950503 <--
WO 1996-US6060 19960501 <--

AB This invention discloses high-affinity oligonucleotide **ligands** to complex tissue targets, specifically nucleic acid **ligands** having the ability to bind to complex tissue targets, and the methods for obtaining such **ligands**. Tissue targets comprise cells, subcellular components, aggregates or cells, collections of cells, and higher ordered structures. Specifically, nucleic acid **ligands** to red blood cell ghosts, glioblastomas, and lymphomas are described.

L79 ANSWER 40 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:39228 HCAPLUS
DN 126:70700
TI From oligonucleotide shapes to genomic **SELEX**: novel biological regulatory loops
AU Gold, Larry; Brown, David; He, Yi-Yuan; Shtatland, Timur; Singer, Britta S.; Wu, Yan
CS Dep. Mol., Cell., Dev. Biol., Univ. Colorado, Boulder, CO, 80309-0347, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1997**), 94(1), 59-64
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal; General Review
LA English
AB A review with 42 refs. The **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) method and oligonucleotide combinatorial chem.

discovery process yields high-affinity/high-specificity **ligands** for virtually any mol. target. Typically, the enormous starting **libraries** used in the **SELEX** process contain 1014-1015 sequences. We now ask if the smaller sequences, complexity of extant organisms, and **evolutionary** history provide useful interactions between oligonucleotides and at least some unexpected targets. I.e., do organisms contain a robust "linkage map" between their oligonucleotides and proteins and/or small mols. that **enriches** life.

L79 ANSWER 41 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:37473 HCAPLUS
DN 126:70808
TI using the **SELEX** combinatorial chemistry process to find high affinity nucleic acid **ligands** to target molecules
AU Tuerk, Craig
CS Morehead State University, Morehead, KY, USA
SO Methods Mol. Biol. (Totowa, N. J.) (**1997**), 67(PCR Cloning Protocols), 219-230
CODEN: MMBIED; ISSN: 1064-3745
PB Humana
DT Journal
LA English
AB Strategy and protocol are presented for the **SELEX** (**Systematic Evolution** of **Ligands** by **Exponential enrichments**) combinatory chem. process by which nucleic acid **ligands** of high affinity can be isolated against a mol. target. The process involves selection and PCR amplification steps repeated until the pool of nucleic acids is dominated by sequences of high affinity for the target mol.

L79 ANSWER 42 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:1251 HCAPLUS
DN 126:112757
TI Bent pseudoknots and novel RNA inhibitors of type 1 human immunodeficiency virus (HIV-1) reverse transcriptase
AU Burke, Donald H.; Scates, Lori; Andrews, Katy; Gold, Larry
CS Department of Mol. Cellular & Dev. Biol., Univ. of Colorado, Boulder, 80309-0347, Colombia
SO J. Mol. Biol. (**1996**), 264(4), 650-666
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic
DT Journal
LA English
AB The reverse transcriptase (RT) of the human immunodeficiency virus (HIV) is a proven target for therapeutic intervention of HIV infections. We have found several new RNA inhibitors of HIV-1 RT that differ significantly from the pseudoknot **ligands** found previously, along with a wide variety of pseudoknot variants. One pseudoknot variant and three novel **ligands** were studied in more detail. Each specifically inhibits DNA polymn. by HIV RT (half-maximal inhibition at 0.3 to 20 nM inhibitor), but not that of RTs derived from MMLV or AMV. The minimal binding element of each isolate was detd. by deletion anal. and by gel electrophoresis of protein-bound, partially alk.-hydrolyzed RNA. Truncations of three of the isolates bound nearly as well as (or better than) the parental sequences, while most deletions in the fourth caused substantial disruption of binding. The truncated versions of two isolates were subjected to six rounds of secondary **SELEX** after resynthesizing them mutagenically. Patterns of conserved, and covarying nucleotides yielded structural models consistent with 5' and 3' boundary detns. for these mols. Among the four isolates studied in detail, the first is confirmed as being a pseudoknot, albeit with substantial structural differences as compared to the canonical pseudoknots identified previously. The second forms a stem-loop structure with addnl. flanking sequences required for binding. Tentative structural models for the other two isolates are presented. The minimal fully active truncations of each of these four isolates compete with each other and with a classical RNA

pseudoknot for binding to HIV RT, suggesting that they all recognize the same or overlapping sites on the protein, in spite of their apparently dissimilar structures. We model their interactions with RT as mimicking the 40 to 45 degree bend in dsDNA co-crystd. with RT.

L79 ANSWER 43 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:538950 HCAPLUS
DN 125:186865
TI Selection of aminoacylated tRNAs from RNA **libraries** having randomized acceptor stem sequences: using old dogs to perform new tricks
AU Sampson, Jeffrey R.; Saks, Margaret E.
CS Div. Biol., California Inst. Technol., Pasadena, CA, 91125, USA
SO Methods Enzymol. (**1996**), 267(Combinatorial Chemistry), 384-410
CODEN: MENZAU; ISSN: 0076-6879
DT Journal
LA English
AB To use **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) to explore whether unique combinations of tRNA acceptor stem nucleotides can functionally mimic the conserved sequence of wild-type Escherichia coli serine tRNAs, it is crit. that the nucleotides at both termini be randomized. An approach was developed that circumvents restrictions on the randomization of the tRNA acceptor stem nucleotides, which entails extending the tRNA 5' and 3' termini to create defined and invariant primer-binding sites and thus allows randomization of the acceptor stem nucleotides such that their recognition by E. coli seryl-tRNA synthetase could be studied using the **SELEX** approach. The general selection scheme is composed of 8 individual steps. (1) A **library** of tRNA mols. having the 5'- hairpin loop is aminoacylated with the synthetase under std. aminoacylation reaction conditions. (2) The total tRNA sample is treated with NaIO4 under acid conditions which will specifically oxidize the 3'-terminal ribose of the unacylated tRNAs. (3) The tRNA sample is treated with 1.0M Tris-Cl, pH 8.2, to remove the amino acid from the acylated tRNAs. (4) The tRNA sample is polyadenylated by poly(A) polymerase (PAP). Because PAP will polyadenylate only those tRNAs having intact 3'-terminal ribose rings, this reaction effectively tags only those tRNAs that had been previously aminoacylated. (5) Complementary DNA specific for the poly(A)-tagged tRNA is obtained by reverse transcription using the 3'-PTBA2 primer. (6) The cDNA is amplified and the T7 promoter is incorporated into the DNA by PCR using the 5'-T7TL and 3'-PTBA2 primers. (7) The PCR product is digested with BsmFI to generate template DNA. (8) The BsmFI-digested DNA is transcribed with T7 RNA polymerase to generate tRNA for the next round of selection. Detailed protocols are provided for each step of this scheme. The steps of the selection scheme, in total or in combination, are generally applicable to other problems that also involve selection for RNA **ligands** that are active for reversible chem. reactions and to situations in which it would be advantageous to randomize the 3'-terminus of an RNA.

L79 ANSWER 44 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:538941 HCAPLUS
DN 125:189680
TI A **SELEX** primer
AU Fitzwater, Tim; Polisky, Barry
CS Nexstar Pharm., Inc., Boulder, CO, 80301, USA
SO Methods Enzymol. (**1996**), 267(Combinatorial Chemistry), 275-301
CODEN: MENZAU; ISSN: 0076-6879
DT Journal; General Review
LA English
AB A review, with 45 refs., of the **SELEX** (**Systematic Evolution** of **Ligands** by **EXponential enrichment**) combinatorial chem. process in drug and diagnostic discovery technol.

L79 ANSWER 45 OF 60 HCAPLUS COPYRIGHT 2000 ACS

AN 1996:466894 HCAPLUS
DN 125:143228
TI Parallel **systematic evolution** of **ligands** by **exponential enrichment** (parallel **SELEX**).
IN Eaton, Bruce; Gold, Larry
PA Nexstar Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9609316	A1	19960328	WO 1995-US11982	19950919 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5723289	A	19980303	US 1994-309245	19940920 <--
	AU 9536795	A1	19960409	AU 1995-36795	19950919 <--
	AU 714469	B2	20000106		
	EP 782580	A1	19970709	EP 1995-934468	19950919 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10508465	T2	19980825	JP 1995-511062	19950919 <--
	US 6030776	A	20000229	US 1997-793398	19970224 <--

PRAI US 1994-309245 19940920 <--
US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
WO 1995-US11982 19950919 <--

AB A method for identifying a product from a product **library**, wherein said product is selected for its ability to perform a preselected function on a target, the method comprising (1) prepg. a nucleic acid-reactant test mixt. composed of nucleic acids each having a region of randomized sequence and each being assocd. with a first reactant, (2) reacting the test mixt. with a free reactant to form a **library** of products, wherein the reaction is facilitated by the nucleic acid assocd. with the first reactant, and (3) partitioning members of the product **library** based on their relative ability to perform their preselected function on a target, whereby said products can be identified. Thus, parallel **SELEX** was carried out involving reaction of 5'-guanosine monophosphorothioate attached to a random RNA 76-mer mixt. (initially approx. 5 .times. 1013 different mols.) with bromoacetylated bradykinin. After 12 rounds, an RNA conjugate was found which showed a 6700-fold increase in kcat/Km for the coupling reaction.

L79 ANSWER 46 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:367011 HCAPLUS
DN 125:51799
TI Calcium-dependent oligonucleotide antagonists specific for L-selectin
AU O'Connell, Dan; Koenig, Andrea; Jennings, Susan; Hicke, Brian; Han, Hui-Ling; Fitzwater, Tim; Chang, Ying-Fon; Varki, Nissi; Parma, David; Varki, Ajit
CS NeXstar Pharmaceuticals Inc., Boulder, CO, 80301, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1996**), 93(12), 5883-5887
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The selectins are calcium-dependent C-type lectins that recognize complex anionic carbohydrate **ligands**, initiating many cell-cell interactions in the vascular **system**. Selectin blockade shows therapeutic promise in a variety of inflammatory and postischemic pathologies. However, the available oligosaccharide **ligand** mimetics have low affinities and show cross-reaction among the three

selectins, precluding efficient and specific blockade. The **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) process uses combinatorial chem. and in vitro selection to yield high affinity oligonucleotides with unexpected binding specificities. Nuclease-stabilized, randomized oligonucleotides subjected to **SELEX** against recombinant L-selectin yielded calcium-dependent antagonists with .apprx.105 higher affinity than the conventional oligosaccharide **ligand** sialyl Lewisx. Most of the isolated **ligands** shared a common consensus sequence. Unlike sialyl Lewisx, these antagonists show little binding to E- or P-selectin. Moreover, they show calcium-dependent binding to native L-selectin on peripheral blood lymphocytes and block L-selectin-dependent interactions with the natural **ligands** on high endothelial venules.

L79 ANSWER 47 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:338232 HCAPLUS
DN 125:1345
TI Production of chimeric nucleic acid molecules involving **systematic evolution** of **ligands** by **exponential enrichment** (**SELEX**)
IN Burke, Donald; Tarasow, Ted; Eaton, Bruce; Gold, Larry
PA University Research Corporation, USA; Nexstar Pharmaceuticals, Inc.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 81

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9604403	A1	19960215	WO 1995-US9446	19950726 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5637459	A	19970610	US 1994-284063	19940802 <--
AU 9531495	A1	19960304	AU 1995-31495	19950726 <--

PRAI US 1994-284063 19940802 <--
US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
WO 1995-US9446 19950726 <--

AB Methods are disclosed for producing chimeric nucleic acid mols. with two or more functionalities. A chimeric **library** is generated in which individual chimeric mols. combine the functions or characteristics of two or more parent **libraries**, each parent **library** having been selected through the **SELEX** procedure for a specific function or feature. The chimeric mols. of this invention are useful in a variety of ways, including having improved affinities for a target mol., enhancing assembly of multicomponent mols., and promoting reactions between two mols., and as diagnostic and therapeutic agents. In an example, chimeric nucleic acid mols. are screened for their ability to cleave the HIV-1 genome in the presence and absence of the tat protein.

L79 ANSWER 48 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:280676 HCAPLUS
DN 124:310961
TI Inhibitory RNA **ligand** to reverse transcriptase from feline immunodeficiency virus
AU Chen, Hang; McBroom, Douglas G.; Zhu, Ya-Qi; Gold, Larry; North, Thomas W.
CS Department of Molecular, University of Colorado, Boulder, CO, 80309, USA
SO Biochemistry (**1996**), 35(21), 6923-6930
CODEN: BICHAW; ISSN: 0006-2960
DT Journal

LA English
AB High-affinity, high-specificity RNA **ligands** for reverse transcriptase from feline immunodeficiency virus (FIV) were isolated from an RNA **library** by the **SELEX** (**Systematic Evolution** of **Ligands** by **EXponential enrichment**) procedure. The selected RNA **ligands** bound to FIV reverse transcriptase with dissocn. consts. in the nanomolar range. One of the **ligands** was a potent inhibitor of the RNA-dependent DNA polymerase activity of both the recombinant and the virion-derived FIV reverse transcriptase. It also inhibited the reverse transcriptase from an FIV mutant that is resistant to 3'-azido-3'-deoxythymidine (AZT). The inhibition of FIV reverse transcriptase was competitive with respect to template-primer and noncompetitive with respect to deoxyribonucleoside 5'-triphosphates. This **ligand** was specific for the FIV enzyme and did not inhibit other reverse transcriptases tested (avian myeloblastosis virus, Moloney murine leukemia virus, and human immunodeficiency virus type 1).

L79 ANSWER 49 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:81598 HCAPLUS
DN 124:222838
TI Himnmgh-affinity **ligands** of insulin receptor antibodies, tachykinin substance P, HIV integrase and HIV-1 reverse transcriptase
IN Gold, Larry; Nieuwlandt, Dan; Wecker, Matthew; Schneider, Daniel J.; Feigon, Juli; Allen, Patrick; Sullenger, Bruce A.; Doudna, Jennifer A.
PA University Research Corp., USA
SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 81

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9530775	A1	19951116	WO 1995-US5600	19950503	<--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ					
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5503978	A	19960402	US 1994-238863	19940506	<--
	US 5648214	A	19970715	US 1994-303362	19940909	<--
	US 5756287	A	19980526	US 1994-361795	19941221	<--
	AU 9524702	A1	19951129	AU 1995-24702	19950503	<--

PRAI US 1994-238863 19940506 <--
US 1994-248632 19940524 <--
US 1994-303362 19940909 <--
US 1994-361795 19941221 <--
US 1990-536428 19900611 <--
US 1991-714131 19910610 <--
US 1992-931473 19920817 <--
US 1992-964624 19921021 <--
US 1993-117911 19930908 <--
US 1993-117991 19930908 <--
WO 1995-US5600 19950503 <--

AB Methods are described for the identification and prepn. of high-affinity **ligands** to insulin receptor antibodies, substance P, HIV integrase and HIV-Reverse Transcriptase. Included in the invention are specific RNA **ligands** to insulin receptor antibodies, substance P and HIV integrase identified by the **SELEX** method. Also included in the invention are ssDNA **ligands** to HIV-1 reverse transcriptase identified by the **SELEX** method. Also included are RNA **ligands** that inhibit the binding of MA-20 to the human insulin receptor, RNA **ligands** that are inhibitors of HIV integrase and ssDNA **ligands** that are inhibitors of HIV-1 reverse

transcriptase.

L79 ANSWER 50 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:13931 HCAPLUS
DN 124:81055
TI Using in vitro selection to direct the covalent attachment of human immunodeficiency virus type 1 Rev protein to high-affinity RNA **ligands**
AU Jensen, Kirk B.; Atkinson, Brent L.; Willis, Michael C.; Koch, Tad H.; Gold, Larry
CS Dep. Mol. Cell. Dev. Biol., Univ. Colorado, Boulder, CO, 80309, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1995**), 92(26), 12220-4
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB We have used an in vitro selection procedure called crosslinking **SELEX** (**SELEX** = **systematic evolution** of **ligands** by **exponential enrichment**) to identify RNA sequences that bind with high affinity and crosslink to the Rev protein from human immunodeficiency virus type 1 (HIV-1). A randomized RNA **library** substituted with the photoreactive chromophore 5-iodouracil was irradiated with monochromatic UV light in the presence of Rev. Those sequences with the ability to photocrosslink to Rev were partitioned from the rest of the RNA pool, amplified, and used for the next round of selection. Rounds of photocrosslinking selection were alternated with rounds of selection for RNA sequences with high affinity to Rev. This iterative, dual-selection method yielded RNA mols. with subnanomolar dissocn. consts. and high efficiency photocrosslinking to Rev. Some of the RNA mols. isolated by this procedure form a stable complex with Rev that is resistant to denaturing gel electrophoresis in the absence of UV irradn. In vitro selection of nucleic acids by using modified nucleotides allows the isolation of nucleic acid mols. with potentially limitless chem. capacities to covalently attack a target mol.

L79 ANSWER 51 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:937813 HCAPLUS
DN 124:79674
TI In vitro selection of RNA **ligands** for the ribosomal L22 protein associated with Epstein-Barr virus-expressed RNA by using randomized and cDNA-derived RNA **libraries**
AU Dobbelstein, Matthias; Shenk, Thomas
CS Howard Hughes Med. Inst., Princeton Univ., Princeton, NJ, 08544-1014, USA
SO J. Virol. (**1995**), 69(12), 8027-34
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The Epstein-Barr virus (EBV)-expressed RNA 1 (EBER1) assocs. tightly with the ribosomal protein L22. We detd. the general requirements for an RNA to bind L22 in a **SELEX** expt., selecting RNA **ligands** for L22 from a randomized pool of RNA sequences by using an L22-glutathione S-transferase fusion protein. The selected sequences all contained a stem-loop motif similar to that of the region of EBER1 previously shown to interact with L22. The nucleotides were highly conserved at three positions within the stem-loop and identical to the corresponding nucleotides in EBER1. Two independent binding sites for L22 could be identified in EBER1, and mobility shift assays indicated that two L22 mols. can interact with EBER1 simultaneously. To search for a cellular L22 **ligand**, we constructed a **SELEX** **library** from cDNA fragments derived from RNA that was coimmunopptd. with L22 from an EBV-neg. whole-cell lysate. After four rounds of selection and amplification, most of the clones that were obtained overlapped a sequence corresponding to the stem-loop between nucleotides 302 and 317 in human 28S rRNA. This stem-loop fulfills the criteria for optimal binding to L22 that were defined by **SELEX**, suggesting that human 28S rRNA is likely to be a cellular L22 **ligand**. Addnl. L22 binding sites were found in 28S rRNA, as well

as within 18S rRNA and in RNA segments not present in sequence databases. The methodol. described for the conversion of a preselected cellular RNA pool into a **SELEX library** might be generally applicable to other proteins for the identification of cellular RNA **ligands**.

L79 ANSWER 52 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:924381 HCAPLUS
TI Therapeutic and diagnostic applications of **SELEX**.
AU Polisky, B.
CS NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SO Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (**1995**), Issue Pt. 2, MEDI-118 Publisher: American Chemical Society, Washington, D. C.
CODEN: 61XGAC
DT Conference; Meeting Abstract
LA English
AB **SELEX** (**Systematic Evolution** of **Ligands** by **EXponential enrichment**) is a combinatorial **ligand** discovery technique that utilizes large random sequence **libraries** comprised of oligonucleotides. These **libraries** are comprised of modified nucleotides that resist degrdn. by nucleases present in plasma. **SELEX** has many applications in new drug discovery and in the development of new diagnostic reagents. Over the past five years it has become apparent that the range of potential **SELEX** targets is vast, ranging from proteins of grater than 100Kd to small org. mols. like ATP and theophylline with MW of 200-300d. Some recent examples of the use of **SELEX** will be described. These include: 1) development of antagonists to intracellular protein targets encoded by HIV including **reverse** transcriptase, Rev and Tat proteins, 2) antagonists to extracellular targets such as proteases involved in inflammation, and angiogenic determinants involved in tumor neovascularization, 3) development of oligonucleotides that interact irreversibly with their targets via the formation of covalent bonds, and 4) development of oligonucleotides that interact with complex targets such as cell surfaces.

L79 ANSWER 53 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:918380 HCAPLUS
DN 124:134748
TI Nuclease-resistant nucleic acid **ligands** to vascular permeability factor/vascular endothelial growth factor
AU Green, Louis S.; Jellinek, Derek; Bell, Carol; Beebe, Laurie A.; Fesitner, Bruce D.; Gill, Stanley C.; Jucker, Fiona M.; Janjic, Nebojsa
CS NeXstar Pharmaceuticals, Boulder, CO, 80301, USA
SO Chem. Biol. (**1995**), 2(10), 683-95
CODEN: CBOLE2; ISSN: 1074-5521
DT Journal
LA English
AB Vascular permeability factor/vascular endothelial growth factor (VPF/VEGF) is a potent inducer of new blood vessel growth (angiogenesis) that contributes to the pathol. of many angiogenesis-assocd. disease states such as psoriasis, rheumatoid arthritis and cancer. Few mol. entities capable of binding to VPF/VEGF with high affinity and specificity have been described to date. Nuclease-resistant 2'-amino-2'-deoxypyrimidine nucleotide RNA (2'-aminopyrimidine RNA) **ligands** that bind to VPF/VEGF with high affinity have been identified by iterative rounds of affinity-selection/amplification from two independent random **libraries**. The sequence information that confers high affinity binding to VPF/VEGF is contained in a contiguous stretch of 24 nucleotides, 5'-ACCCUGAUGGUAGACGCCGGGGUG-3' (2'-aminopyridimidine nucleotides are designated with bold-face letters). Of the 14 ribopurines in this minimal **ligand**, 10 can be substituted with the corresponding 2'-O-methylpurine nucleotides without a redn. in binding affinity to VPF/VEGF. In fact, the 2'-O-Me substitution at permissive positions leads to a .apprx.17-fold improvement in the binding affinity to

VPF/VEGEF. The higher affinity results from the redn. in the dissocn. rate const. of the 2'-O-methyl-substituted RNA **ligand** from the protein compared to the unsubstituted **ligand**. The 2'-O-methyl-substituted minimal **ligand** which folds into a bulged hairpin motif, is also more thermally stable than the unsubstituted **ligand**. Nuclease resistance of the **ligand** is further improved by the 2'-O-Me substitutions and the addn. of short phosphorothioate caps to the 3'- and 5'-ends. In conclusion, the **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) process in conjunction with post-**SELEX** modifications was used to define a highly nuclease-resistant oligonucleotide that binds to VPF/VEGF with high affinity and specificity.

L79 ANSWER 54 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:764106 HCAPLUS
DN 123:330726
TI Potent 2'-Amino-2'-deoxypyrimidine RNA Inhibitors of Basic Fibroblast Growth Factor
AU Jellinek, Derek; Green, Louis S.; Bell, Carol; Lynott, C. Kate; Gill, Nicole; Vargeese, Chandra; Kirschenheuter, Gary; McGee, Daniel P. C.; Abesinghe, Padmapriya; et al.
CS NeXstar Pharmaceuticals Inc., Boulder, CO, 80301, USA
SO Biochemistry (**1995**), 34(36), 11363-72
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Screening of random oligonucleotide **libraries** with **SELEX** [**systematic evolution** of **ligands** by **exponential enrichment**] has emerged as a powerful method for identifying high-affinity nucleic acid **ligands** for a wide range of mol. targets. Nuclease sensitivity of unmodified RNA and DNA, however, imposes considerable restrictions on their use as therapeutics or diagnostics. Modified RNA in which pyrimidine 2'-hydroxy groups have been substituted with 2'-amino groups (2'-aminopyrimidine RNA) is known to be substantially more resistant to serum nucleases. The authors report here on the use of **SELEX** to identify high-affinity 2-aminopyrimidine RNA **ligands** to a potent angiogenic factor, basic fibroblast growth factor (bFGF). High-affinity **ligands** with the same consensus primary structure have been isolated from two independent **libraries** of approx. 6.times.1014 mols. contg. 30 or 50 randomized positions. Compared to unmodified RNA with the same sequence, 2'-aminopyrimidine **ligands** are at least 1000-fold more stable in 90% human serum. The sequence information required for high-affinity binding to bFGF is contained within 24-26 nucleotides. The minimal **ligand** m21A (5'-GGUGUGUGGAAGACAGCGGGUGGUUC-3'; G = guanosine, A = adenosine, C = 2'-amino-2'-deoxycytidine, U = 2'-amino-2'-deoxyuridine, and C = 2'-amino-2'-deoxycytidine or deoxycytidine) binds to bFGF with an apparent dissocn. const. (Kd) of (3.5 .times. 0.3) .times. 10-10 M at 37.degree. in phosphate = buffered saline (pH 7.4). Dissocn. of m21A from bFGF is adequately described with a first-order rate const. of (1.96) .times. 10-3 s-1 (t1/2 = 5.9 min). The calcd. value for the assocn. rate const. (kon = koff/Kd) was 5.6.times.106 M-1 s-1. Highly specific binding of m21A to bFGF was obsd.: binding to denatured bFGF, five proteins from the FGF family (acidic FGF, FGF-4, FGF-5, FGF-6, and FGF-7), and four other heparin binding proteins is substantially weaker under the same conditions with KdbFGF/Kdprotein values ranging from (4.1) .times. 10-2 to >10-6. Heparin but not chondroitin sulfate competed for binding of m21A to bFGF. In cell culture, m21A inhibited [125I]bFGF binding to both low-affinity sites (ED50 .apprxeq. 1 nM) and high-affinity sites (ED50 .apprxeq. 3 nM) on CHO cells expressing transfected FGF receptor-1. Basic FGF-dependent migration of bovine aortic endothelial cells as well as bFGF-induced proliferation of human umbilical vein endothelial cells was also inhibited by m21A in a concn.-dependent manner with ED50 values of 50-100 nM. The 2'-aminopyrimidine RNA **ligand** m21A therefore represents a useful lead compd. in the efforts to develop potent

oligonucleotide-based angiogenesis antagonists.

L79 ANSWER 55 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:683095 HCAPLUS
DN 123:74263
TI High-affinity ssDNA inhibitors of the reverse transcriptase of type 1 human immunodeficiency virus
AU Schneider, Daniel J.; Feigon, Juli; Hostomsky, Zdenek; Gold, Larry
CS Department of MCD Biology, University of Colorado, Boulder, CO, 80309, USA
SO Biochemistry (**1995**), 34(29), 9599-610
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB The reverse transcriptase (RT) of HIV-1 is a plausible target for therapeutic agents aimed at inhibiting propagation of the virus. We have used "irrational drug design", i.e., combinatorial chem. with oligonucleotide **libraries**, to identify high-affinity **ligands** aimed at HIV-1 RT. The methodol., termed **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**), was employed with a single-stranded DNA **library**. The selected ssDNA **ligands** bind HIV-1 RT with Kd values as low as 1 nM and inhibit the RNA-dependent DNA-polymerase activity of the enzyme with Ki values as low as 0.3 nM. We also demonstrate the high specificity of one **ligand** able to selectively discriminate between the reverse transcriptases of HIV-1, AMV, and MMLV. These ssDNA mols. may be useful as inhibitors or as models for the design of small mol. inhibitors of HIV-1 RT in vivo.

L79 ANSWER 56 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:679947 HCAPLUS
DN 123:77272
TI Diversity of oligonucleotide functions
AU Gold, Larry; Polisky, Barry; Uhlenbeck, Olke; Yarus, Michael
CS NeXstar Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SO Annu. Rev. Biochem. (**1995**), 64, 763-97
CODEN: ARBOAW; ISSN: 0066-4154
DT Journal; General Review
LA English
AB A review with 138 refs. **SELEX** is a technol. for the identification of high affinity oligonucleotide **ligands**. Large **libraries** of random sequence single-stranded oligonucleotides, whether RNA or DNA, can be thought of conformationally not as short strings but rather as sequence dependent folded structures with high degrees of mol. rigidity in soln. This conformational complexity means that such a **library** is a source of high affinity **ligands** for a surprising variety of mol. targets, including nucleic acid binding proteins such as polymerases and transcription factors, non-nucleic acid binding proteins such as cytokines and growth factors, as well as small org. mols. such as ATP and theophylline. The range of applications of this technol. for new discovery extends from basic research reagents to the identification of novel diagnostic and therapeutic reagents. Examples of these applications are described along with a discussion of underlying principles and future developments expected to further the utility of **SELEX**.

L79 ANSWER 57 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:673845 HCAPLUS
DN 121:273845
TI Heterofunctional proteins and their use as affinity reagents
IN Kay, Brian K.; Fowlkes, Dana M.
PA University of North Carolina, USA
SO PCT Int. Appl., 256 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9418318	A1	19940818	WO 1994-US977	19940201 <--
	W: CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5498538	A	19960312	US 1993-176500	19931230 <--
	US 5747334	A	19980505	US 1994-189331	19940131 <--
	EP 689590	A1	19960103	EP 1994-907345	19940201 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08506487	T2	19960716	JP 1994-518106	19940201 <--

PRAI	US 1993-13416	19930201	<--
	US 1993-176500	19931230	<--
	US 1994-189331	19940131	<--
	US 1990-480420	19900215	<--
	US 1992-854133	19920319	<--
	WO 1994-US977	19940201	<--

AB A novel method for the prepn. of improved heterofunctional binding fusion proteins termed Totally Synthetic Affinity Reagents (TSARs) is described. These proteins are useful in diagnostics and therapeutics (no data). TSARs are concatenated heterofunctional proteins with at least two functional regions: a binding domain with affinity for a **ligand** and a second effector peptide portion that is chem. or biol. active and preferably connected via an optionally labile linker peptide. A **library** of chimeric genes encoding the biol. active peptide at one end of the gene with the other end made up of random **oligonucleotides** is **screened** by activity for constructs that bind the desired **ligand**. The construction and characterization of a no. of **libraries** in M13 using the pIII gene to ensure presentation of the random **oligonucleotide** -encoded domains and the **screening** of two of these **libraries** for **ligands** for a monoclonal antibody to a prostate carcinoma-specific antigen (mAb 7E11-C5) are demonstrated.

L79 ANSWER 58 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:573645 HCAPLUS
DN 121:173645
TI Selection of high-affinity RNA **ligands** to reverse transcriptase: Inhibition of cDNA synthesis and RNase H activity
AU Chen, Hang; Gold, Larry
CS Department of Molecular Cellular and Developmental Biology, University of Colorado, Boulder, CO, 80309, USA
SO Biochemistry (**1994**), 33(29), 8746-56
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Specific, high-affinity RNA **ligands** to avian myeloblastosis virus and Moloney murine leukemia virus reverse transcriptases were isolated from a combinatorial RNA **library** using the **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) procedure. The selected RNA **ligands** bound their resp. reverse transcriptases with approx. nanomolar dissocn. consts. The **ligands** did not exhibit primary sequence conservation from selections against different target enzymes. Moreover, the selected **ligands** competed with the binding of template/primer complex and inhibited both the RNA-dependent DNA polymerase and the RNase H activities of the cognate reverse transcriptase. **SELEX** can yield both high-affinity and high-specificity oligonucleotide antagonists against specific members of a protein family.

L79 ANSWER 59 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:531953 HCAPLUS
DN 121:131953
TI Inhibition of receptor binding by high-affinity RNA **ligands** to vascular endothelial growth factor
AU Jellinek, Derek; Green, Louis S.; Bell, Carol; Janjic, Nebojsa

CS Nexagen Inc., Boulder, CO, 80301, USA
SO Biochemistry (**1994**), 33(34), 10450-6
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB The proliferation of new blood vessels (angiogenesis) is a process that accompanies many pathol. conditions including rheumatoid arthritis and solid tumor growth. Among angiogenic cytokines that have been identified to date, vascular endothelial growth factor (VEGF) is one of the most potent. **SELEX** (**systematic evolution** of **ligands** by **exponential enrichment**) was used to identify RNA **ligands** that bind to VEGF in a specific manner with affinities in the low nanomolar range. **Ligands** were selected from a starting pool of .apprx.1014 RNA mols. contg. 30 randomized positions. Isolates from the affinity-**enriched** pool were grouped into 6 distinct families on the basis of primary and secondary structure similarities. Minimal sequence information required for high-affinity binding to VEGF is contained in 29-36-nucleotide motifs. Binding of truncated (minimal) high-affinity **ligands** to VEGF is competitive with that of other truncated **ligands** and heparin. Furthermore, truncated **ligands** from the 6 **ligand** families inhibit binding of [125I]VEGF to its cell-surface receptors. Oligonucleotide **ligands** described here represent an initial set of lead compds. in the ongoing effort toward the development of potent and specific VEGF antagonists.

L79 ANSWER 60 OF 60 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:54943 HCAPLUS
DN 120:54943
TI An **unnatural** biopolymer
AU Cho, Charles Y.; Moran, Edmund J.; Cherry, Sara R.; Stephans, James C.; Fodor, Stephen P. A.; Adams, Cynthia L.; Sundaram, Arathi; Jacobs, Jeffrey W.; Schultz, Peter G.
CS Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
SO Science (Washington, D. C., 1883-) (**1993**), 261(5126), 1303-5
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB A highly efficient method has been developed for the solid-phase synthesis of an "**unnatural** biopolymer" consisting of chiral aminocarbonate monomers linked via a carbamate backbone. Oligocarbamates were synthesized from N-protected p-nitrophenyl carbonate monomers, substituted with a variety of side chains, with greater than 99 percent overall coupling efficiencies per step. A spatially defined **library** of oligocarbamates was generated by using photochem. methods and screened for binding affinity to a monoclonal antibody. A no. of high-affinity **ligands** were then synthesized and analyzed in soln. with respect to their inhibition concn. values, water/octanol partitioning coeffs., and proteolytic stability. These and other **unnatural** polymers may provide new frameworks for drug development and for testing theories of protein and peptide folding and structure.

=> d his 180-

FILE 'HCAPLUS' ENTERED AT 10:29:46 ON 27 MAR 2000
L80 11 S L51 AND TRANSITION (3A) METAL
L81 6 S L51 AND ?ORGANOMETAL?
L82 14 S L80,L81
L83 3 S L51 AND (MULTISTAG? OR MULTIEQUILIB? OR MULTI()(STAG? OR EQUI
L84 6 S L51 AND (SELFASSEMBL? SELFAMPLIF? OR SELF()(ASSEMBL? OR AMPLI
L85 9 S L83,L84

L86 20 S L82,L85 NOT L31,L79
L87 0 S L68 AND IMIN?

=> d bib abs tot 186

L86 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:784329 HCAPLUS
DN 132:20781
TI Optical amplification of molecular interactions using liquid crystals
IN Abbott, Nicholas L.; Skaife, Justin J.; Gupta, Vinay K.; Dubrovsky, Timothy B.; Shah, Rahul
PA The Regents of the University of California, USA
SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9963329	A1	19991209	WO 1999-US12540	19990604 <--

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1998-92453 19980605 <--
US 1998-127382 19980731 <--
OS MARPAT 132:20781
AB App. is described which comprises a first substrate having a surface, the surface comprising a recognition moiety; a mesogenic layer oriented on the surface; and an interface between the mesogenic layer and a member selected from the group consisting of gases, liqs. solids and combinations thereof. A second substrate may be provided over the mesogenic moiety. The app. may be specifically configured for use for detecting an interaction between an analyte and a recognition moiety by detecting changes in the orientation of the mesogens occurring as a result of the interaction. Methods for detecting an analyte are described which entail contacting a recognition moiety for an analyte with a sample so that, when the analyte of interest is present, the contacting causes at least a portion of a plurality of mesogens proximate to the recognition moiety to detectably switch from a first orientation to a second orientation upon contacting the analyte with the recognition moiety; and detecting the second configuration. The analyte may be selected from the group consisting of acids, bases, org. ions, inorg. ions, pharmaceuticals, herbicides, pesticides, chem. warfare agents, noxious gases, biomols., and combinations of these. App. for synthesizing and screening a **library** of compds. is also described which comprises a synthesis component, comprising a first substrate having a surface, and a **self-assembled** monolayer on the surface, the monolayer comprising a reactive functionality; and an anal. component, comprising: a second substrate having a surface, and a mesogenic layer between the surface of the first substrate and the surface of the second substrate. **Libraries** of compds. synthesized on a **self-assembled** monolayer are also claimed, as are low energy surfaces (surface energy 1-40 mJ/m2) with mesogenic layers anchored on them. Methods for controlling the tilt of, and/or optical texture in a mesogenic layer anchored to, a haloorganosulfur moiety adsorbed on a substrate entail controlling the halogen content of the moiety.

L86 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:530850 HCAPLUS
TI Using molecular mechanics to aid catalyst design
AU Landis, Clark R.; Wright, John M.
CS Department Chemistry, University Wisconsin, Madison, WI, 53706, USA
SO Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (**1998**), ORGN-488 Publisher: American Chemical Society, Washington, D. C.

CODEN: 66KYA2
DT Conference; Meeting Abstract
LA English
AB An alternative approach to the discovery of new enantiospecific catalysts via screening of combinatorial **libraries** is computer-aided rational design. A potentially fruitful area for the application of computer-aided methods is the rational design of new chiral **ligands** to be attached to catalytically active **transition metal** centers. Recently Ito coined the term "secondary interactions" to describe control of specificity in such catalysts that arises from attractive interactions (e.g. hydrogen bonding, covalent attachments, etc.) that occur outside the primary coordination sphere of the **transition metal**. In this talk we will discuss the design of asym. phosphine **ligands** that incorporate functional groups that can interact with complementary functional groups of a substrate to create a secondary interaction. The synthesis, structure, and catalytic properties of catalysts contg. these **ligands** will be described also.

L86 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:467748 HCAPLUS
DN 129:183309
TI Metal complexes with biologically important **ligands**, Part 100. **Bioorganometallic** chemistry-**transition metal** complexes with .alpha.-amino acids and peptides
AU Severin, Kay; Bergs, Ralph; Beck, Wolfgang
CS Institut Anorganische Chemie, Universitat, Munchen, D-80333, Germany
SO Angew. Chem., Int. Ed. (**1998**), 37(12), 1635-1654
CODEN: ACIEF5; ISSN: 1433-7851
PB Wiley-VCH Verlag GmbH
DT Journal; General Review
LA English
AB The theme of this review article, with over 174 refs., is **organometallic** complexes of the **transition metals** with .alpha.-amino acids and peptides. This branch of **bioorganometallic** chem. may be viewed as the logical next step in the classical coordination chem. of .alpha.-amino acid and peptide **ligands**. However, the special physicochem. properties of these compds. also permit some completely new applications, the potential of interdisciplinary research being reflected in the diversity of these applications: .alpha.-amino acids and peptides and their derivs. can not only be synthesized, labeled, and stabilized by **organometallic** complexes, they can also be activated. This is exploited, for example, in the synthesis of .alpha.-amino acids with unusual side chains and led to the development of an immunoassay based on carbonyl complexes as well as to a template-controlled synthesis of peptides on chiral half-sandwich complexes (synthetic ribosomes). .alpha.-Amino acid and peptide **ligands** also find extended use in enantioselective catalysis. As a consequence of their modular character peptides are of particular interest as **ligands** for catalyst **libraries**.

L86 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:436615 HCAPLUS
DN 129:175153
TI Combinatorial **libraries** of **transition-metal** complexes, catalysts and materials
AU Francis, Matthew B.; Jamison, Timothy F.; Jacobsen, Eric N.
CS Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SO Curr. Opin. Chem. Biol. (**1998**), 2(3), 422-428
CODEN: COCBF4; ISSN: 1367-5931
PB Current Biology Ltd.
DT Journal; General Review
LA English
AB The design, synthesis and evaluation of **transition metal** contg. combinatorial **libraries** has received much attention in

the past few years. As a result, a variety of synthetic techniques were developed, and rapid assays for metal ion binding have yielded new **ligand** classes displaying high affinity and selectivity. Research in catalysis has centered around lead optimization using much smaller parallel **libraries** because of the lack of a truly efficient reaction screening method. Materials science applications have also focused on spatially addressed **libraries** and have employed a variety of techniques to identify compds. with desired phys. properties. Nonetheless, high-throughput characterization and reaction product detection methods must still be developed to realize the full potential of combinatorial chem. for the discovery of novel metal-contg. compds. A review with 19 refs.

L86 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:235215 HCAPLUS
DN 128:235608
TI Accelerated syntheses and screening of stereoselective **transition metal** catalysts
AU Burgess, Kevin; Porte, Alex M.
CS Department of Chemistry, Texas AandM University, College Station, TX, USA
SO Adv. Catal. Processes (**1997**), 2(Asymmetric Catalysis), 69-82
CODEN: ACPRFB
PB JAI Press Inc.
DT Journal; General Review
LA English
AB A review with 58 refs. on topics of: parallel in the biotechnol. and pharmaceutical industries, evolution of methods for generation and screening of **transition metal** catalyst **libraries**, **libraries** of **transition metal** complexes: demonstration of high throughput screening, easily constructed **ligands**, divergent **ligand** syntheses, solid phrase syntheses of **ligands**.

L86 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:215668 HCAPLUS
DN 129:2294
TI Optical amplification of **ligand**-receptor binding using liquid crystals
AU Gupta, Vinay K.; Skaife, Justin J.; Dubrovsky, Timothy B.; Abbott, Nicholas L.
CS Dep. Chemical Eng. and Materials Science, Univ. California, Davis, CA, 95616, USA
SO Science (Washington, D. C.) (**1998**), 279(5359), 2077-2080
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB Liq. crystals (LCs) were used to amplify and transduce receptor-mediated binding of proteins at surfaces into optical outputs. Spontaneously organized surfaces were designed so that protein mols., upon binding to **ligands** hosted on these surfaces, triggered changes in the orientations of 1- to 20-.mu.m-thick films of supported LCs, thus corresponding to a reorientation of .apprx.105 to 106 mesogens per protein. Binding-induced changes in the intensity of light transmitted through the LC were easily seen with the naked eye and could be further amplified by using surfaces designed so that protein-**ligand** recognition causes twisted nematic LCs to untwist. This approach to the detection of **ligand**-receptor binding does not require labeling of the analyte, does not require the use of electroanal. app., provides a spatial resoln. of micrometers, and is sufficiently simple that it may find use in biochem. assays and imaging of spatially resolved chem. **libraries**.

L86 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:745938 HCAPLUS
DN 128:29690

TI **Organometallic ligands** for the localization and quantification of amyloid in vivo and in vitro
IN Lansbury, Peter T., Jr.; Han, Hogyu; Cho, Cheon-gyu; Zhen, Weiguo; Harper, James D.; Davison, Alan
PA Massachusetts Institute of Technology, USA; Brigham and Women's Hospital, Inc.
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741856	A1	19971113	WO 1997-US7792	19970507 <--

PI W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1996-16599 19960508 <--
US 1997-38999 19970225 <--
OS MARPAT 128:29690
AB Novel **transition metal** complexes, in particular 99Tc complexes, with azo dye derivs. providing a Nx or Ny,Sz donor set for binding amyloid are described. Methods using such compds. for detg. by imaging the localization or quantification of amyloid fibrils in a mammal, for diagnosing the degree of progression of Alzheimer's disease in a mammal, for monitoring the response to therapy in a mammal having Alzheimer's disease, for identifying an agent useful for treating Alzheimer's disease, for treating Alzheimer's disease, and for detecting the presence of the infectious form of the prion protein, are also described.

L86 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:727283 HCAPLUS
DN 127:302450
TI **Self-Assembly** of Tetra- and Hexanuclear Circular Helicates
AU Hasenknopf, Bernold; Lehn, Jean-Marie; Boumediene, Nedjia; Dupont-Gervais, Annick; Van Dorsselaer, Alain; Kneisel, Boris; Fenske, Dieter
CS Laboratoire de Chimie Supramoleculaire and the Laboratoire de Spectrometrie de Masse Bio-Organique, Universite Louis Pasteur, Strasbourg, 67000, Fr.
SO J. Am. Chem. Soc. (**1997**), 119(45), 10956-10962
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The **self-assembly** of the tris-bipyridine **ligands** BI (5,5'-bis[2-(5'-methyl-2,2'-bipyridin-5-yl)ethyl]2,2'-bipyridine) and BII (5,5'-bis[(5'-methyl-2,2'-bipyridin-5-yl)methoxymethyl]2,2'-bipyridine) with iron(II) salts yields polynuclear complexes displaying structures of cyclic double-helix type, termed circular helicates [n]cH (of order n). With BI, in which the bipyridine units in the **ligand** are connected by ethylene bridges, penta- or hexanuclear architectures [5]cH ([Fe5BI5]10+) and [6]cH ([Fe6BI6]12+) were obtained, depending on the anion present during the **self-assembly** process. The elongated tris-bipyridine **ligand** BII with oxypropylene bridges forms a tetranuclear circular helicate [4]cH ([Fe4BII4](PF6)8), whose structure was confirmed by crystal structure detn. as a solvate (tetragonal, space group P4/n, R1 = 0.1178). The possible oligomeric combinations of tris-bipy **ligands** and iron(II) ions may be considered to constitute the potential members of a virtual combinatorial **library**, generated via dynamic combinatorial chem., from which a specific real constituent of the virtual set of circular helicates is expressed in given conditions.

L86 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:658793 HCAPLUS

DN 127:342381
TI Detection and isolation of RNA-binding proteins by RNA-**ligand** screening of a cDNA expression **library**
AU Sagesser, Rudolf; Martinez, Emilio; Tsagris, Mina; Tabler, Martin
CS Foundation for Research and Technology-Hellas, Institute of Molecular Biology and Biotechnology, Heraklion, GR-71110, Greece
SO Nucleic Acids Res. (**1997**), 25(19), 3816-3822
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB A screening assay for the detection of RNA-binding proteins was developed. It allows the rapid isolation of cDNA clones coding for proteins with sequence-specific binding affinity to a target RNA. For developing the screening protocol, constituents of the human U1 snRNP were utilized as model system. The RNA partner consisted of the U1-RNA stem loop II and the corresponding protein consisted of the 102 amino acid N-terminal recognition motif of the U1A protein, which was fused to .beta.-galactosidase and expressed by the recombinant lambda phage LU1A. Following binding of the fusion protein to nitrocellulose membranes, hybridization with a 32P-labeled U1-RNA **ligand** was carried out to detect specific RNA-protein interaction. Parameters influencing the specificity and the detection limit of binding were systematically investigated with the aid of the model system. Processing the nitrocellulose membranes in the presence of **transition metals** greatly increased the signal:background ratio. A simple screening protocol involving a single-buffer system was developed. Specific RNA-protein interaction could be detected in the presence of a large excess of recombinant phages from a cDNA **library**. Only moderate binding affinities (Kd = 10-8 M) were required. The suitability of the RNA-**ligand** screening protocol was demonstrated by the identification of new viroid-RNA binding proteins from tomato.

L86 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:521585 HCAPLUS
DN 127:217270
TI New mass spectrometric methods for the study of noncovalent associations of biopolymers
AU Smith, Richard D.; Bruce, James E.; Wu, Qinyuan; Lei, Q. Paula
CS Environmental Molecular Sciences Laboratory, Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SO Chem. Soc. Rev. (**1997**), 26(3), 191-202
CODEN: CSRVBR; ISSN: 0306-0012
PB Royal Society of Chemistry
DT Journal
LA English
AB The use of electrospray ionization-mass spectrometry (ESI-MS) for the characterization of noncovalent complexes of biomacromols. in soln. is based upon the gentle nature of the electrospray process that allows a wide range of assocns. to be transferred intact to the gas phase as fully desolvated complexes. Examples include multimeric proteins, oligonucleotide duplexes, DNA-drug complexes and enzyme-inhibitor complexes. Various studies have indicated that at least some qualities of the three-dimensional soln. structures are retained in the gas phase. Recent investigations have also shown the relative stabilities of complexes in the gas phase can be very different than the same complexes in soln. In spite of this, the use of very gentle electrospray interface conditions can provide a direct reflection of relative soln. abundances for similar complexes. Competitive binding expts. using sets of **ligands** have been shown to yield insights regarding relative binding affinities in soln. The potential for high throughput affinity screening of combinatorial **libraries** using ESI-MS is described based upon the **multi-stage** MS capability of Fourier transform ion cyclotron resonance instrumentation and involving the characterization of components (after dissocn.) of the **library** constituents initially present as complexes with a target biopolymer in

the ion trap. This approach combines, in one rapid expt., both affinity selection by complex formation with a biopolymer and the identification of the **ligands** selected from combinatorial mixts., thus providing information on the relative binding affinities of the **library** constituents. The present status, limitations and promise of these methods are discussed.

L86 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:487760 HCAPLUS
TI Design of a modular **library** of **ligand** pieces for metal-containing liquid crystals.
AU Workman, Jose M.; Clements, Martin J.; Hummel, Matthew T.; Jessie, Benjamin C.; McCarty, Melissa A.; Mullins, Richard J.
CS Department Chemistry, Centre College, Danville, KY, 40422, USA
SO Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (**1997**), INOR-361 Publisher: American Chemical Society, Washington, D. C.
CODEN: 64RNAO
DT Conference; Meeting Abstract
LA English
AB We have initiated a research program in the synthesis of **transition metal**-contg. liq. crystals. Our main focus to this point has been the construction of a modular **library** of **ligand** pieces. The **ligand** pieces have features that are desirable for making metal-contg. liq. crystals. They possess flat, arom. portions, flexible alkyl chains, and different coordination sites. We combine the pieces to make a large no. of **ligands** that differ slightly in structure. Because of the **library** of pieces, promising **ligands** can be modified easily. There are three basic **ligand** types: polyanionic chelating (I), Jager-type (II), and Salen (III). All of these are tetradentate N2O2 donors and we are investigating the coordination of first-row **transition metals**. We anticipate forming both thermotropic and lyotropic liuqid crystals. The liq. cryst. properties of the **ligands** and metal complexes are under investigation.

L86 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:166031 HCAPLUS
DN 126:247939
TI De novo design of heterotrimeric coiled coils
AU Lombardi, Angela; Bryson, James W.; DeGrado, William F.
CS Centro Interdipartimentate Ricerca Peptidi Bioattivi, University Napoli "Federico II", Naples, 80134, Italy
SO Biopolymers (**1997**), Volume Date 1996, 40(5), 495-504
CODEN: BIPMAA; ISSN: 0006-3525
PB Wiley
DT Journal
LA English
AB The three-helix bundle is a common structural motif among natural proteins. It has been obsd. in numerous important proteins, such as fibrinogen, laminin, spectrin, dystrophin, hemagglutinin, and mannose binding proteins. The three-helix bundle is a simple structure in which three .alpha.-helix pack against each other, with a slight left-handed twist. Because of its simplicity relative to other structural motifs, the three-helix bundle can be conveniently used both to clarify the forces responsible for the protein folding and stability, and for the design of novel proteins. In this paper we describe the design, synthesis, and characterization of three peptides that **self-assemble** into antiparallel, heterotrimeric coiled coils. The exptl. results, obtained from CD spectroscopy and ultracentrifugation equil. sedimentation, indicate that the mixt. of the three peptides preferentially forms heterotrimers; moreover, these aggregates represent attractive systems for combinatorial design of **libraries** of pseudo C3 sym. **ligands** or binding sites.

L86 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2000 ACS

AN 1996:565314 HCAPLUS
DN 125:214588
TI All D-amino acid hexapeptide inhibitors of melittin's cytolytic activity derived from synthetic combinatorial **libraries**
AU Blondelle, Sylvie E.; Houghten, Richard A.; Perez-Paya, Enrique
CS Torrey Pines Inst. Mol. Studies, San Diego, CA, 92121, USA
SO J. Mol. Recognit. (**1996**), 9(2), 163-168
CODEN: JMORE4; ISSN: 0952-3499
DT Journal
LA English
AB The identification of peptides that inhibit the biol. functions of proteins was used as a means to explore protein/**ligand** interactions involved in mol. recognition processes. This approach is based on the use of synthetic combinatorial **libraries** (SCLs) for the rapid identification of individual peptides that block the interaction of proteins with their biol. targets. Thus, each peptide mixt. of an all-D-amino acid hexapeptide SCL in a positional scanning format was screened for its ability to inhibit the hemolytic activity of melittin, a model **self-assembling** protein. The potent inhibitory activity of the identified individual peptides suggests that protein-like complexes are able to specifically bind to peptides having an all-D configuration. These results also show that SCLs are useful for the identification of short, non-hydrolyzable sequences having potential intracellular inhibitory activities.

L86 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:544189 HCAPLUS
DN 125:236878
TI Combinatorial Approach to the Discovery of Novel Coordination Complexes
AU Francis, Matthew B.; Finney, Nathaniel S.; Jacobsen, Eric N.
CS Department of Chemistry, Harvard University, Cambridge, MA, 02138, USA
SO J. Am. Chem. Soc. (**1996**), 118(37), 8983-8984
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB Metal complexes are reported as formed using a **library** from combinatorial chem. The **library** was prepd. on poly(ethylene glycol)-grafted polystyrene so that each polymer bead displayed a unique **ligand** structure. The **library** theor. consisted of 12,000 different **ligands**. It comprises 4 variable components: 2 amino acids linked by a "turn element" and terminated by various capping reagents. The turn elements employed were cyclic 1,2-amino alcs. or .alpha.-amino acid derivs. Metals used were Ni, Fe, Cu, Pt, Sn, and Pd. With Ni, 4 different **ligands** were found each bearing L-His(Trt) in both amino acid positions; only 2 turn elements, acetyl and 1-naphthylenyl chlorides, were found. Extent of binding is reported for the other metals with some general observations regarding selectivity of amino acids.

L86 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:529887 HCAPLUS
DN 125:178497
TI **Libraries** of **transition-metal** catalysts: high-throughput screening of catalysts for synthetic organic methodology
AU Burgess, Kevin; Moye-Sherman, Destardi; Porte, Alex M.
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77843-3255, USA
SO Mol. Diversity Comb. Chem.: Libr. Drug Discovery, Conf. (**1996**), 128-136. Editor(s): Chaiken, Irwin M.; Janda, Kim D. Publisher: American Chemical Society, Washington, D. C.
CODEN: 63HMAW
DT Conference; General Review
LA English
AB A review with 31 refs.; high throughput screening of catalysts is described. Batches of up to 96 different catalyst systems were established simultaneously, then screened sequentially. This technol. has been applied to a C-H insertion and a cyclopropanation reaction; several

interesting results emerged, notably silver-based optically active catalysts. The scope of high throughput screening is currently limited by the no. of catalysts and catalyst precursors that are conveniently available. Therefore, synthesis of a new phosphine **ligand** type was performed, illustrating a scheme which can be adjusted to give many related **ligands**. It is anticipated that high throughput screens of such a series of **ligands** will facilitate fine-turning of catalyst properties.

L86 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:231355 HCAPLUS
DN 122:4971
TI Random chemistry for the generation of new compounds
IN Kauffman, Stuart A.; Rebek, Julius, Jr.
PA USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9424314	A1	19941027	WO 1994-US4314	19940419 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2160457	AA	19941027	CA 1994-2160457	19940419 <--
AU 9468158	A1	19941108	AU 1994-68158	19940419 <--
EP 695368	A1	19960207	EP 1994-916542	19940419 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09500007	T2	19970107	JP 1994-523552	19940419 <--
AU 9880020	A1	19981022	AU 1998-80020	19980814 <--

PRAI US 1993-49268 19930419 <--
WO 1994-US4314 19940419 <--

AB Methods for the generation of new compds. are disclosed. The present invention eliminates the need to know in advance the structure or chem. compn. of a compd. having a desired property. The disclosure of the present invention provides that diversity of unknown compds. may be produced by "random" chem., and such a diversity of unknown compds. may be screened for one or more desired properties to detect the presence of suitable compds. In one aspect, a starting group of org. compds. is caused to undergo a series of chem. reactions to create a diversity of new org. compds. that are screened for the presence of org. compds. having the desired property. In another aspect of the present invention, a diversity of compds. is generated from a group of substrates which are subjected to group of enzymes representing a diversity of catalytic activities. The methodol. of the invention may be used to produce drugs, vaccines, etc. Prepn. of ubiquitin fusion **libraries** with diversity of 1 x 107, as well as generation of a diversity of product mols., are described.

L86 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:503633 HCAPLUS
DN 121:103633
TI Complex combinatorial chemical **libraries** encoded with tags
IN Still, W. Clark; OHL-Meyer, Michael H. J.; Wigler, Michael; Dillard, Lawrence; Reader, John
PA Columbia University, USA; Cold Spring Harbor Lab.
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9408051 A1 19940414 WO 1993-US9345 19931001 <--
W: AT, AU, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KR, LU, NL, NO, NZ, PL, RO, RU, SE, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, PT, SE
EP 665897 A1 19950809 EP 1994-900350 19931001 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
HU 72495 A2 19960528 HU 1995-952 19931001 <--
JP 08506175 T2 19960702 JP 1993-509330 19931001 <--
AU 686579 B2 19980212 AU 1994-55369 19931001 <--
NO 9501230 A 19950330 NO 1995-1230 19950330 <--
US 6001579 A 19991214 US 1995-485018 19950607 <--
AU 9745258 A1 19980212 AU 1997-45258 19971117 <--
PRAI US 1992-955371 19921001 <--
US 1993-13948 19930204 <--
US 1993-130271 19931001 <--
WO 1993-US9345 19931001 <--
US 1993-159861 19931130 <--
US 1994-227007 19940413 <--
OS MARPAT 121:103633
AB Methods and compns. are provided for encoded combinatorial chem., whereby at each stage of the synthesis, a support such as a particle upon which a compd. is being synthesized is uniquely tagged to define a particular event, usually chem., assocd. with the synthesis of the compd. on the support. The tagging is accomplished using identifier mols. which record the sequential events to which the supporting particle is exposed during synthesis, thus providing a reaction history for the compd. produced on the support. Various products can be produced in the **multi-stage** synthesis, such as oligomers and synthetic nonrepetitive org. mols. Conveniently, nested families of compds. can be employed as identifiers, where no. and/or position of a substituent define the choice. Alternatively, detectable functionalities may be employed, such as radioisotopes, fluorescers, halogens, and the like, where presence and ratios of two different groups can be used to define stage or choice. Particularly, pluralities of identifiers may be used to provide a binary or higher code, so as to define a plurality of choices with only a few detachable tags. The particles may be screened for a characteristic of interest, particularly binding affinity, where the products may be detached from the particle or retained on the particle. The reaction history of the particles which are pos. for the characteristic can be detd. by the release of the tags and anal. to define the reaction history of the particle. An encoded combinatorial **library** of 2401 peptides was prepd. (by solid phase synthesis) having the sequence (X4)EEDLGGGG (X = Asp, Glu, Ile, Lys, Leu, Gln, or Ser). The 4 Gly served as a spacer between the encoded amino acid sequence and the bead. The **library** included the sequence KLISEEDL, part of the epitope bound by monoclonal antibody 9E10 to the human C-myc gene product. The identifiers used were 2-nitro-4-carboxybenzyl O-aryl-substituted .omega.-hydroxyalkyl carbonates (aryl = pentachlorophenyl, 2,4,6-trichlorophenyl, or 2,6-dichloro-4-fluorophenyl) and were attached via their carboxylic acids to tag free amino groups on each bead. The tags were released from each selected bead by photolysis, silylated, and analyzed by electron capture gas chromatog. The binary synthesis code of the bead was directly detd. from the chromatogram of the tags.

L86 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:131562 HCAPLUS
DN 120:131562
TI Two-stage selection of sequences from a random phage display **library** delineates both core residues and permitted structural range within an epitope
AU Miceli, Robert M.; DeGraaf, Michael E.; Fischer, H. David
CS Molecular Biology Research, The Upjohn Company, 301 Henrietta Street, Kalamazoo, MI, 49007, USA
SO J. Immunol. Methods (**1994**), 167(1-2), 279-87
CODEN: JIMMBG; ISSN: 0022-1759
DT Journal

LA English
AB **Libraries** of random peptides can be screened to identify species which interact with antibodies or receptors. Similarly, maps of native mol. interactions can frequently be deduced by screening a limited set of peptide fragments derived from sequences within a native antigen or **ligand**. However, the existence of cross-reactive sequences that mimic original epitopes and the limited replaceability of amino acid residues suggest that the sequence space accessible by a receptor can be much broader. Definition of this space is of particular importance where structural information is required for peptidomimetic or drug design. The authors have used a two-stage selection scheme to expand the sequence space accessible by a phage display **library** and to define peptide epitopes of the anti-FLAG octapeptide monoclonal M2 antibody. Affinity selection of a primary **library** of 2.times.106 random decapeptides identified a non-contiguous core of three residues in the binding motif Tyr-Lys-Xaa-Xaa-Asp. A second stage **library** with 2.times.107 individual clones bearing the core motif but with the remaining flanking and internal residues re-randomized permitted access to a broader sequence space represented in a **library** equiv. to several orders of magnitude larger. Data demonstrate that extended access to binding sequence space permitted by **multi-stage** screening of phage display **libraries** can reveal not only essential residues required for **ligand** binding, but also the **ligand** structural range permitted within the receptor binding pocket.

L86 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1992:145126 HCAPLUS
DN 116:145126
TI Identification and characterization of a Saccharomyces cerevisiae gene (PAR1) conferring resistance to iron chelators
AU Schnell, Norbert; Entian, Karl Dieter
CS Inst. Mikrobiol., Johann Wolfgang Goethe-Univ. Frankfurt, Frankfurt/Main, W-6000, Germany
SO Eur. J. Biochem. (**1991**), 200(2), 487-93
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB o-Phenanthroline (1,10-phenanthroline) is a chem. known to chelate iron and other **transition metal** ions. This compd. was added to solid yeast media to reduce the concn. of biol. available iron. Other essential divalent cations, like Zn2+ or Cu2+, which could also be bound, were supplemented. Growth of wild-type yeast strains was totally inhibited at specific concns. of the chelator. However, several cells contg. plasmid of a multicopy vector genomic **library** of S. cerevisiae could be selected by growth on the these media. All of the resistant clones carried a single addnl. gene, PAR1 on their multicopy plasmids. Plasmid-directed overexpression of PAR1 increased the resistance of transformants to o-phenanthroline and addnl. conferred resistance to 1-nitroso-2-naphthaol, an iron(III)-binding mol. with different coordinating **ligands**. By supplementing the o-phenanthroline-contg. media with several different metal ions, it could be proved that the selection plates really caused a specific iron limitation. These observations clearly demonstrated that the overexpressed PAR1 gene enables the cell to complete with iron-chelating org. mols. PAR1 Null mutants, constructed by insertion of the LEU2 gene into the open reading frame, showed a remarkable phenotype: they did not grow on slightly alk. buffered media (pH >7) and became hypersensitive to oxidative stress by hydrogen peroxide. Of several heavy metal ions, such as Fe3+, Fe2+, Co2+, Ni2+, Cu2+ and Zn2+, tested for supplementation of the alk. growth deficiency, only iron, either added in the ferrous or ferric form, was able to restore cell growth. It can be concluded from the DNA sequence that PAR1 encodes a highly acidic protein of 650 residues with mostly hydrophilic character. Some interesting repetitive amino acid motifs, such as (Asp-Arg)4 or Cys-Ser-Glu, may act as metal-binding sites. The possible role of PAR1 is discussed.

L86 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2000 ACS
AN 1981:441592 HCAPLUS
DN 95:41592
TI Theoretical **organometallic** chemistry
AU Hoffmann, Roald
CS USA
SO Science (Washington, D. C., 1883-) (**1981**), 211(4486), 995-1002
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal; General Review
LA English
AB **Organometallic** chemists have synthesized a remarkable variety of new structural types. In these structures **ligands**, which are org. or inorg. mols. of variable independent stability, bind to one or more **transition metal** atoms. An approach to an understanding of the electronic structure, geometrical preferences, and reactivity of these complexes may be made if the mol. is "decompd." conceptually into a metal fragment, MLn, and a **ligand**. A **library** of the mol. orbitals of these fragments is becoming available. One then "reconstructs" the mol. by examg. the interaction of the orbitals of the **ligand**, typically an org. mol., with the orbitals of the MLn fragment. A review with many refs.